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(54) Title: NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

(57) Abstract: The present invention provides novel nucleic acids, novel polypeptide sequences encoded by these nucleic acids and uses thereof.

NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

1. TECHNICAL FIELD

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with uses for these polynucleotides and proteins, for example in therapeutic, diagnostic and research methods.

2. BACKGROUND

Technology aimed at the discovery of protein factors (including e.g., cytokines, such as lymphokines, interferons, CSFs, chemokines, and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (i.e., partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization-based cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity, for example, by virtue of their secreted nature in the case of leader sequence cloning, by virtue of their cell or tissue source in the case of PCR-based techniques, or by virtue of structural similarity to other genes of known biological activity.

Identified polynucleotide and polypeptide sequences have numerous applications in, for example, diagnostics, forensics, gene mapping; identification of mutations responsible for genetic disorders or other traits, to assess biodiversity, and to produce many other types of data and products dependent on DNA and amino acid sequences.

3. SUMMARY OF THE INVENTION

The compositions of the present invention include novel isolated polypeptides, novel isolated polynucleotides encoding such polypeptides, including recombinant DNA

molecules, cloned genes or degenerate variants thereof, especially naturally occurring variants such as allelic variants, antisense polynucleotide molecules, and antibodies that specifically recognize one or more epitopes present on such polypeptides, as well as hybridomas producing such antibodies.

The compositions of the present invention additionally include vectors, including expression vectors, containing the polynucleotides of the invention, cells genetically engineered to contain such polynucleotides and cells genetically engineered to express such polynucleotides.

The present invention relates to a collection or library of at least one novel nucleic acid sequence assembled from expressed sequence tags (ESTs) isolated mainly by sequencing by hybridization (SBH), and in some cases, sequences obtained from one or more public databases. The invention relates also to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. These nucleic acid sequences are designated as SEQ ID NO: 1-739. The polypeptides sequences are designated SEQ ID NO: 740-1478. The nucleic acids and polypeptides are provided in the Sequence Listing. In the nucleic acids provided in the Sequence Listing, A is adenosine; C is cytosine; G is guanine; T is thymine; and N is any of the four bases. In the amino acids provided in the Sequence Listing, * corresponds to the stop codon.

The nucleic acid sequences of the present invention also include, nucleic acid sequences that hybridize to the complement of SEQ ID NO:1-739 under stringent hybridization conditions; nucleic acid sequences which are allelic variants or species homologues of any of the nucleic acid sequences recited above, or nucleic acid sequences that encode a peptide comprising a specific domain or truncation of the peptides encoded by SEQ ID NO:1-739. A polynucleotide comprising a nucleotide sequence having at least 90% identity to an identifying sequence of SEQ ID NO:1-739 or a degenerate variant or fragment thereof. The identifying sequence can be 100 base pairs in length.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO:1-739. The sequence information can be a segment of any one of SEQ ID NO:1-739 that uniquely identifies or represents the sequence information of SEQ ID NO:1-739.

A collection as used in this application can be a collection of only one polynucleotide. The collection of sequence information or identifying information of each sequence can be provided on a nucleic acid array. In one embodiment, segments of sequence information is provided on a nucleic acid array to detect the polynucleotide that contains the segment. The array can be designed to detect full-match or mismatch to the polynucleotide that contains the segment. The collection can also be provided in a computer-readable format.

This invention also includes the reverse or direct complement of any of the nucleic acid sequences recited above; cloning or expression vectors containing the nucleic acid sequences; and host cells or organisms transformed with these expression vectors. Nucleic acid sequences (or their reverse or direct complements) according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology, such as use as hybridization probes, use as primers for PCR, use in an array, use in computer-readable media, use in sequencing full-length genes, use for chromosome and gene mapping, use in the recombinant production of protein, and use in the generation of anti-sense DNA or RNA, their chemical analogs and the like.

In a preferred embodiment, the nucleic acid sequences of SEQ ID NO:1-739 or novel segments or parts of the nucleic acids of the invention are used as primers in expression assays that are well known in the art. In a particularly preferred embodiment, the nucleic acid sequences of SEQ ID NO:1-739 or novel segments or parts of the nucleic acids provided herein are used in diagnostics for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The isolated polynucleotides of the invention include, but are not limited to, a polynucleotide comprising any one of the nucleotide sequences set forth in SEQ ID NO:1-739; a polynucleotide comprising any of the full length protein coding sequences of SEQ ID NO:1 - 739; and a polynucleotide comprising any of the nucleotide sequences of the mature protein coding sequences of SEQ ID NO: 1- 739. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent hybridization conditions to (a) the complement of any one of the nucleotide sequences set forth in SEQ ID NO:1-739; (b) a nucleotide sequence encoding any one of the

amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotides recited above; (d) a polynucleotide which encodes a species homolog (e.g. orthologs) of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of any of the polypeptides comprising an amino acid sequence set forth in the Sequence Listing.

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising any of the amino acid sequences set forth in the Sequence Listing; or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides with biological activity that are encoded by (a) any of the polynucleotides having a nucleotide sequence set forth in SEQ ID NO:1-739; or (b) polynucleotides that hybridize to the complement of the polynucleotides of (a) under stringent hybridization conditions. Biologically or immunologically active variants of any of the polypeptide sequences in the Sequence Listing, and "substantial equivalents" thereof (e.g., with at least about 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid sequence identity) that preferably retain biological activity are also contemplated. The polypeptides of the invention may be wholly or partially chemically synthesized but are preferably produced by recombinant means using the genetically engineered cells (e.g. host cells) of the invention.

The invention also provides compositions comprising a polypeptide of the invention. Polypeptide compositions of the invention may further comprise an acceptable carrier, such as a hydrophilic, e.g., pharmaceutically acceptable, carrier.

The invention also provides host cells transformed or transfected with a polynucleotide of the invention.

The invention also relates to methods for producing a polypeptide of the invention comprising growing a culture of the host cells of the invention in a suitable culture medium under conditions permitting expression of the desired polypeptide, and purifying the polypeptide from the culture or from the host cells. Preferred embodiments include those in which the protein produced by such process is a mature form of the protein.

Polynucleotides according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology. These techniques include use as hybridization probes, use as oligomers, or primers, for PCR, use for chromosome and gene mapping, use in the recombinant production of protein,

and use in generation of anti-sense DNA or RNA, their chemical analogs and the like. For example, when the expression of an mRNA is largely restricted to a particular cell or tissue type, polynucleotides of the invention can be used as hybridization probes to detect the presence of the particular cell or tissue mRNA in a sample using, *e.g., in situ* hybridization.

In other exemplary embodiments, the polynucleotides are used in diagnostics as expressed sequence tags for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The polypeptides according to the invention can be used in a variety of conventional procedures and methods that are currently applied to other proteins. For example, a polypeptide of the invention can be used to generate an antibody that specifically binds the polypeptide. Such antibodies, particularly monoclonal antibodies, are useful for detecting or quantitating the polypeptide in tissue. The polypeptides of the invention can also be used as molecular weight markers, and as a food supplement.

Methods are also provided for preventing, treating, or ameliorating a medical condition which comprises the step of administering to a mammalian subject a therapeutically effective amount of a composition comprising a polypeptide of the present invention and a pharmaceutically acceptable carrier.

In particular, the polypeptides and polynucleotides of the invention can be utilized, for example, in methods for the prevention and/or treatment of disorders involving aberrant protein expression or biological activity.

The present invention further relates to methods for detecting the presence of the polynucleotides or polypeptides of the invention in a sample. Such methods can, for example, be utilized as part of prognostic and diagnostic evaluation of disorders as recited herein and for the identification of subjects exhibiting a predisposition to such conditions. The invention provides a method for detecting the polynucleotides of the invention in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the polynucleotide of interest for a period sufficient to form the complex and under conditions sufficient to form a complex and detecting the complex such that if a complex is detected, the polynucleotide of interest is detected. The

invention also provides a method for detecting the polypeptides of the invention in a sample comprising contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex and detecting the formation of the complex such that if a complex is formed, the polypeptide is detected.

The invention also provides kits comprising polynucleotide probes and/or monoclonal antibodies, and optionally quantitative standards, for carrying out methods of the invention. Furthermore, the invention provides methods for evaluating the efficacy of drugs, and monitoring the progress of patients, involved in clinical trials for the treatment of disorders as recited above.

The invention also provides methods for the identification of compounds that modulate (i.e., increase or decrease) the expression or activity of the polynucleotides and/or polypeptides of the invention. Such methods can be utilized, for example, for the identification of compounds that can ameliorate symptoms of disorders as recited herein. Such methods can include, but are not limited to, assays for identifying compounds and other substances that interact with (*e.g.*, bind to) the polypeptides of the invention. The invention provides a method for identifying a compound that binds to the polypeptides of the invention comprising contacting the compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and detecting the complex by detecting the reporter gene sequence expression such that if expression of the reporter gene is detected the compound the binds to a polypeptide of the invention is identified.

The methods of the invention also provides methods for treatment which involve the administration of the polynucleotides or polypeptides of the invention to individuals exhibiting symptoms or tendencies. In addition, the invention encompasses methods for treating diseases or disorders as recited herein comprising administering compounds and other substances that modulate the overall activity of the target gene products. Compounds and other substances can effect such modulation either on the level of target gene/protein expression or target protein activity.

The polypeptides of the present invention and the polynucleotides encoding them are also useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in Table 2). If no homology is set forth for a sequence, then the polypeptides and polynucleotides of the present invention are useful for a variety of applications, as described herein, including use in arrays for detection.

4. DETAILED DESCRIPTION OF THE INVENTION

4.1 DEFINITIONS

It must be noted that as used herein and in the appended claims, the singular forms "a", "an" and "the" include plural references unless the context clearly dictates otherwise.

The term "active" refers to those forms of the polypeptide which retain the biologic and/or immunologic activities of any naturally occurring polypeptide. According to the invention, the terms "biologically active" or "biological activity" refer to a protein or peptide having structural, regulatory or biochemical functions of a naturally occurring molecule. Likewise "immunologically active" or "immunological activity" refers to the capability of the natural, recombinant or synthetic polypeptide to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The term "activated cells" as used in this application are those cells which are engaged in extracellular or intracellular membrane trafficking, including the export of secretory or enzymatic molecules as part of a normal or disease process.

The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence 5'-AGT-3' binds to the complementary sequence 3'-TCA-5'. Complementarity between two single-stranded molecules may be "partial" such that only some of the nucleic acids bind or it may be "complete" such that total complementarity exists between the single stranded molecules. The degree of complementarity between the nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands.

The term "embryonic stem cells (ES)" refers to a cell that can give rise to many differentiated cell types in an embryo or an adult, including the germ cells. The term "germ line stem cells (GSCs)" refers to stem cells derived from primordial stem cells that provide a steady and continuous source of germ cells for the production of gametes. The term "primordial germ cells (PGCs)" refers to a small population of cells set aside from other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during embryogenesis that have the potential to differentiate into germ cells and other cells. PGCs are the source from which GSCs and ES cells are derived The PGCs, the GSCs and the ES cells are capable of self-renewal. Thus these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells that comprise the adult specialized organs, but are able to regenerate themselves.

The term "expression modulating fragment," EMF, means a series of nucleotides which modulates the expression of an operably linked ORF or another EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are nucleic acid fragments which induce the expression of an operably linked ORF in response to a specific regulatory factor or physiological event.

The terms "nucleotide sequence" or "nucleic acid" or "polynucleotide" or "oligonculeotide" are used interchangeably and refer to a heteropolymer of nucleotides or the sequence of these nucleotides. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA) or to any DNA-like or RNA-like material. In the sequences herein A is adenine, C is cytosine, T is thymine, G is guanine and N is A, C, G or T (U). It is contemplated that where the polynucleotide is RNA, the T (thymine) in the sequences provided herein is substituted with U (uracil). Generally, nucleic acid segments provided by this invention may be assembled from fragments of the genome and short oligonucleotide linkers, or from a series of oligonucleotides, or from individual nucleotides, to provide a synthetic nucleic acid

which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon, or a eukaryotic gene.

The terms "oligonucleotide fragment" or a "polynucleotide fragment", "portion," or "segment" or "probe" or "primer" are used interchangeably and refer to a sequence of nucleotide residues which are at least about 5 nucleotides, more preferably at least about 7 nucleotides, more preferably at least about 9 nucleotides, more preferably at least about 11 nucleotides and most preferably at least about 17 nucleotides. The fragment is preferably less than about 500 nucleotides, preferably less than about 200 nucleotides, more preferably less than about 100 nucleotides, more preferably less than about 50 nucleotides and most preferably less than 30 nucleotides. Preferably the probe is from about 6 nucleotides to about 200 nucleotides, preferably from about 15 to about 50 nucleotides, more preferably from about 17 to 30 nucleotides and most preferably from about 20 to 25 nucleotides. Preferably the fragments can be used in polymerase chain reaction (PCR), various hybridization procedures or microarray procedures to identify or amplify identical or related parts of mRNA or DNA molecules. A fragment or segment may uniquely identify each polynucleotide sequence of the present invention. Preferably the fragment comprises a sequence substantially similar to any one of SEQ ID NOs:1-20.

Probes may, for example, be used to determine whether specific mRNA molecules are present in a cell or tissue or to isolate similar nucleic acid sequences from chromosomal DNA as described by Walsh et al. (Walsh, P.S. et al., 1992, PCR Methods Appl 1:241-250). They may be labeled by nick translation, Klenow fill-in reaction, PCR, or other methods well known in the art. Probes of the present invention, their preparation and/or labeling are elaborated in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY; or Ausubel, F.M. et al., 1989, Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, both of which are incorporated herein by reference in their entirety.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO:1-739. The sequence information can be a segment of any one of SEQ ID NO:1-739 that uniquely identifies or represents the sequence information of that sequence of SEQ ID NO:1-739. One such segment can be a twenty-mer nucleic acid sequence because the probability that a twenty-

mer is fully matched in the human genome is 1 in 300. In the human genome, there are three billion base pairs in one set of chromosomes. Because 4^{20} possible twenty-mers exist, there are 300 times more twenty-mers than there are base pairs in a set of human chromosomes. Using the same analysis, the probability for a seventeen-mer to be fully matched in the human genome is approximately 1 in 5. When these segments are used in arrays for expression studies, fifteen-mer segments can be used. The probability that the fifteen-mer is fully matched in the expressed sequences is also approximately one in five because expressed sequences comprise less than approximately 5% of the entire genome sequence.

Similarly, when using sequence information for detecting a single mismatch, a segment can be a twenty-five mer. The probability that the twenty-five mer would appear in a human genome with a single mismatch is calculated by multiplying the probability for a full match ($1 \div 4^{25}$) times the increased probability for mismatch at each nucleotide position (3 x 25). The probability that an eighteen mer with a single mismatch can be detected in an array for expression studies is approximately one in five. The probability that a twenty-mer with a single mismatch can be detected in a human genome is approximately one in five.

The term "open reading frame," ORF, means a series of nucleotide triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

The terms "operably linked" or "operably associated" refer to functionally related nucleic acid sequences. For example, a promoter is operably associated or operably linked with a coding sequence if the promoter controls the transcription of the coding sequence. While operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements e.g. repressor genes are not contiguously linked to the coding sequence but still control transcription/translation of the coding sequence.

The term "pluripotent" refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism. A pluripotent cell is restricted in its differentiation capability in comparison to a totipotent cell.

The terms "polypeptide" or "peptide" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof and to

naturally occurring or synthetic molecules. A polypeptide "fragment," "portion," or "segment" is a stretch of amino acid residues of at least about 5 amino acids, preferably at least about 7 amino acids, more preferably at least about 9 amino acids and most preferably at least about 17 or more amino acids. The peptide preferably is not greater than about 200 amino acids, more preferably less than 150 amino acids and most preferably less than 100 amino acids. Preferably the peptide is from about 5 to about 200 amino acids. To be active, any polypeptide must have sufficient length to display biological and/or immunological activity.

The term "naturally occurring polypeptide" refers to polypeptides produced by cells that have not been genetically engineered and specifically contemplates various polypeptides arising from post-translational modifications of the polypeptide including, but not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation.

The term "translated protein coding portion" means a sequence which encodes for the full length protein which may include any leader sequence or any processing sequence.

The term "mature protein coding sequence" means a sequence which encodes a peptide or protein without a signal or leader sequence. The "mature protein portion" means that portion of the protein which does not include a signal or leader sequence. The peptide may have been produced by processing in the cell which removes any leader/signal sequence. The mature protein portion may or may not include the initial methionine residue. The methionine residue may be removed from the protein during processing in the cell. The peptide may be produced synthetically or the protein may have been produced using a polynucleotide only encoding for the mature protein coding sequence.

The term "derivative" refers to polypeptides chemically modified by such techniques as ubiquitination, labeling (e.g., with radionuclides or various enzymes), covalent polymer attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which do not normally occur in human proteins.

The term "variant"(or "analog") refers to any polypeptide differing from naturally occurring polypeptides by amino acid insertions, deletions, and substitutions, created using, *e g.*, recombinant DNA techniques. Guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest, may be found by comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology (conserved regions) or by replacing amino acids with consensus sequence.

Alternatively, recombinant variants encoding these same or similar polypeptides may be synthesized or selected by making use of the "redundancy" in the genetic code. Various codon substitutions, such as the silent changes which produce various restriction sites, may be introduced to optimize cloning into a plasmid or viral vector or expression in a particular prokaryotic or eukaryotic system. Mutations in the polynucleotide sequence may be reflected in the polypeptide or domains of other peptides added to the polypeptide to modify the properties of any part of the polypeptide, to change characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate.

Preferably, amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, *i.e.*, conservative amino acid replacements. "Conservative" amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Insertions" or "deletions" are preferably in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation allowed may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using recombinant DNA techniques and assaying the resulting recombinant variants for activity.

Alternatively, where alteration of function is desired, insertions, deletions or non-conservative alterations can be engineered to produce altered polypeptides. Such alterations can, for example, alter one or more of the biological functions or biochemical characteristics of the polypeptides of the invention. For example, such alterations may change polypeptide characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate. Further, such alterations can be selected so as to generate polypeptides that are better suited for expression, scale up and the like in the host cells chosen for expression. For example, cysteine residues can be deleted or substituted with another amino acid residue in order to eliminate disulfide bridges.

The terms "purified" or "substantially purified" as used herein denotes that the indicated nucleic acid or polypeptide is present in the substantial absence of other biological macromolecules, *e.g.*, polynucleotides, proteins, and the like. In one embodiment, the polynucleotide or polypeptide is purified such that it constitutes at least 95% by weight, more preferably at least 99% by weight, of the indicated biological macromolecules present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 1000 daltons, can be present).

The term "isolated" as used herein refers to a nucleic acid or polypeptide separated from at least one other component (e.g., nucleic acid or polypeptide) present with the nucleic acid or polypeptide in its natural source. In one embodiment, the nucleic acid or polypeptide is found in the presence of (if anything) only a solvent, buffer, ion, or other component normally present in a solution of the same. The terms "isolated" and "purified" do not encompass nucleic acids or polypeptides present in their natural source.

The term "recombinant," when used herein to refer to a polypeptide or protein, means that a polypeptide or protein is derived from recombinant (*e.g.*, microbial, insect, or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (e.g., yeast) expression systems. As a product, "recombinant microbial" defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, *e.g.*, *E. coli*, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern in general different from those expressed in mammalian cells.

The term "recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. An expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription initiation and termination sequences. Structural units intended for use in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an amino terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

The term "recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extrachromosomally. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed. This term also means host cells which have stably integrated a recombinant genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers. Recombinant expression systems as defined herein will express polypeptides or proteins endogenous to the cell upon induction of the regulatory elements linked to the endogenous DNA segment or gene to be expressed. The cells can be prokaryotic or eukaryotic.

The term "secreted" includes a protein that is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence when it is expressed in a suitable host cell. "Secreted" proteins include without limitation proteins secreted wholly (*e.g.*, soluble proteins) or partially (*e.g.*, receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins that are transported across the membrane of the endoplasmic reticulum. "Secreted" proteins are also intended to include proteins containing non-typical signal sequences (e.g. Interleukin-1 Beta, see Krasney, P.A. and Young, P.R. (1992) Cytokine 4(2):134

-143) and factors released from damaged cells (e.g. Interleukin-1 Receptor Antagonist, see Arend, W.P. et. al. (1998) Annu. Rev. Immunol. 16:27-55)

Where desired, an expression vector may be designed to contain a "signal or leader sequence" which will direct the polypeptide through the membrane of a cell. Such a sequence may be naturally present on the polypeptides of the present invention or provided from heterologous protein sources by recombinant DNA techniques.

The term "stringent" is used to refer to conditions that are commonly understood in the art as stringent. Stringent conditions can include highly stringent conditions (i.e., hybridization to filter-bound DNA in 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1X SSC/0.1% SDS at 68°C), and moderately stringent conditions (i.e., washing in 0.2X SSC/0.1% SDS at 42°C). Other exemplary hybridization conditions are described herein in the examples.

In instances of hybridization of deoxyoligonucleotides, additional exemplary stringent hybridization conditions include washing in 6X SSC/0.05% sodium pyrophosphate at 37°C (for 14-base oligonucleotides), 48°C (for 17-base oligos), 55°C (for 20-base oligonucleotides), and 60°C (for 23-base oligonucleotides).

As used herein, "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. Typically, such a substantially equivalent sequence varies from one of those listed herein by no more than about 35% (*i.e.*, the number of individual residue substitutions, additions, and/or deletions in a substantially equivalent sequence, as compared to the corresponding reference sequence, divided by the total number of residues in the substantially equivalent sequence is about 0.35 or less). Such a sequence is said to have 65% sequence identity to the listed sequence. In one embodiment, a substantially equivalent, *e.g.*, mutant, sequence of the invention varies from a listed sequence by no more than 30% (70% sequence identity); in a variation of this embodiment, by no more than 25% (75% sequence identity); and in a further variation of this embodiment, by no more than 20% (80% sequence identity) and in a further variation of this embodiment, by no more than 10% (90% sequence identity) and in a further variation of this embodiment,

by no more that 5% (95% sequence identity). Substantially equivalent, *e.g.*, mutant, amino acid sequences according to the invention preferably have at least 80% sequence identity with a listed amino acid sequence, more preferably at least 90% sequence identity. Substantially equivalent nucleotide sequences of the invention can have lower percent sequence identities, taking into account, for example, the redundancy or degeneracy of the genetic code. Preferably, nucleotide sequence has at least about 65% identity, more preferably at least about 75% identity, and most preferably at least about 95% identity. For the purposes of the present invention, sequences having substantially equivalent biological activity and substantially equivalent expression characteristics are considered substantially equivalent. For the purposes of determining equivalence, truncation of the mature sequence (*e.g.*, via a mutation which creates a spurious stop codon) should be disregarded. Sequence identity may be determined, e.g., using the Jotun Hein method (Hein, J. (1990) Methods Enzymol. 183:626-645). Identity between sequences can also be determined by other methods known in the art, e.g. by varying hybridization conditions.

The term "totipotent" refers to the capability of a cell to differentiate into all of the cell types of an adult organism.

The term "transformation" means introducing DNA into a suitable host cell so that the DNA is replicable, either as an extrachromosomal element, or by chromosomal integration. The term "transfection" refers to the taking up of an expression vector by a suitable host cell, whether or not any coding sequences are in fact expressed. The term "infection" refers to the introduction of nucleic acids into a suitable host cell by use of a virus or viral vector.

As used herein, an "uptake modulating fragment," UMF, means a series of nucleotides which mediate the uptake of a linked DNA fragment into a cell. UMFs can be readily identified using known UMFs as a target sequence or target motif with the computer-based systems described below. The presence and activity of a UMF can be confirmed by attaching the suspected UMF to a marker sequence. The resulting nucleic acid molecule is then incubated with an appropriate host under appropriate conditions and the uptake of the marker sequence is determined. As described above, a UMF will increase the frequency of uptake of a linked marker sequence.

Each of the above terms is meant to encompass all that is described for each, unless the context dictates otherwise.

4.2 NUCLEIC ACIDS OF THE INVENTION

Nucleotide sequences of the invention are set forth in the Sequence Listing.

The isolated polynucleotides of the invention include a polynucleotide comprising the nucleotide sequences of SEQ ID NO:1-739 ; a polynucleotide encoding any one of the peptide sequences of SEQ ID NO:740-1478; and a polynucleotide comprising the nucleotide sequence encoding the mature protein coding sequence of the polypeptides of any one of SEQ ID NO:740-1478. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent conditions to (a) the complement of any of the nucleotides sequences of SEQ ID NO:1-739 ; (b) nucleotide sequences encoding any one of the amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotide recited above; (d) a polynucleotide which encodes a species homolog of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of the polypeptides of SEQ ID NO: 740-1478. Domains of interest may depend on the nature of the encoded polypeptide; e.g., domains in receptor-like polypeptides include ligand-binding, extracellular, transmembrane, or cytoplasmic domains, or combinations thereof; domains in immunoglobulin-like proteins include the variable immunoglobulin-like domains; domains in enzyme-like polypeptides include catalytic and substrate binding domains; and domains in ligand polypeptides include receptor-binding domains.

The polynucleotides of the invention include naturally occurring or wholly or partially synthetic DNA, e.g., cDNA and genomic DNA, and RNA, e.g., mRNA. The polynucleotides may include all of the coding region of the cDNA or may represent a portion of the coding region of the cDNA.

The present invention also provides genes corresponding to the cDNA sequences disclosed herein. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification

and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. Further 5' and 3' sequence can be obtained using methods known in the art. For example, full length cDNA or genomic DNA that corresponds to any of the polynucleotides of SEQ ID NO:1-739 can be obtained by screening appropriate cDNA or genomic DNA libraries under suitable hybridization conditions using any of the polynucleotides of SEQ ID NO:1-739 or a portion thereof as a probe. Alternatively, the polynucleotides of SEQ ID NO:1-739 may be used as the basis for suitable primer(s) that allow identification and/or amplification of genes in appropriate genomic DNA or cDNA libraries.

The nucleic acid sequences of the invention can be assembled from ESTs and sequences (including cDNA and genomic sequences) obtained from one or more public databases, such as dbEST, gbpri, and UniGene. The EST sequences can provide identifying sequence information, representative fragment or segment information, or novel segment information for the full-length gene.

The polynucleotides of the invention also provide polynucleotides including nucleotide sequences that are substantially equivalent to the polynucleotides recited above. Polynucleotides according to the invention can have, *e.g.*, at least about 65%, at least about 70%, at least about 75%, at least about 80%, more typically at least about 90%, and even more typically at least about 95%, sequence identity to a polynucleotide recited above.

Included within the scope of the nucleic acid sequences of the invention are nucleic acid sequence fragments that hybridize under stringent conditions to any of the nucleotide sequences of SEQ ID NO:1-739, or complements thereof, which fragment is greater than about 5 nucleotides, preferably 7 nucleotides, more preferably greater than 9 nucleotides and most preferably greater than 17 nucleotides. Fragments of, e.g. 15, 17, or 20 nucleotides or more that are selective for (i.e. specifically hybridize to any one of the polynucleotides of the invention) are contemplated. Probes capable of specifically hybridizing to a polynucleotide can differentiate polynucleotide sequences of the invention from other polynucleotide sequences in the same family of genes or can differentiate human genes from genes of other species, and are preferably based on unique nucleotide sequences.

The sequences falling within the scope of the present invention are not limited to these specific sequences, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequence provided SEQ ID NO:1-739, a representative fragment thereof, or a nucleotide sequence at least 90% identical, preferably 95% identical, to SEQ ID NO:1-739 with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another codon that encodes the same amino acid is expressly contemplated.

The nearest neighbor or homology result for the nucleic acids of the present invention, including SEQ ID NO:1-739, can be obtained by searching a database using an algorithm or a program. Preferably, a BLAST which stands for Basic Local Alignment Search Tool is used to search for local sequence alignments (Altshul, S.F. J Mol. Evol. 36 290-300 (1993) and Altschul S.F. et al. J. Mol. Biol. 21:403-410 (1990)). Alternatively a FASTA version 3 search against Genpept, using Fastxy algorithm.

Species homologs (or orthologs) of the disclosed polynucleotides and proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous or related to that encoded by the polynucleotides.

The nucleic acid sequences of the invention are further directed to sequences which encode variants of the described nucleic acids. These amino acid sequence variants may be prepared by methods known in the art by introducing appropriate nucleotide changes into a native or variant polynucleotide. There are two variables in the construction of amino acid sequence variants: the location of the mutation and the nature of the mutation. Nucleic acids encoding the amino acid sequence variants are preferably constructed by mutating the polynucleotide to encode an amino acid sequence that does not occur in nature. These nucleic acid alterations can be made at sites that differ in the

nucleic acids from different species (variable positions) or in highly conserved regions (constant regions). Sites at such locations will typically be modified in series, *e.g.*, by substituting first with conservative choices (*e.g.*, hydrophobic amino acid to a different hydrophobic amino acid) and then with more distant choices (*e.g.*, hydrophobic amino acid to a charged amino acid), and then deletions or insertions may be made at the target site. Amino acid sequence deletions generally range from about 1 to 30 residues, preferably about 1 to 10 residues, and are typically contiguous. Amino acid insertions include amino- and/or carboxyl-terminal fusions ranging in length from one to one hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Intrasequence insertions may range generally from about 1 to 10 amino residues, preferably from 1 to 5 residues. Examples of terminal insertions include the heterologous signal sequences necessary for secretion or for intracellular targeting in different host cells and sequences such as FLAG or poly-histidine sequences useful for purifying the expressed protein.

In a preferred method, polynucleotides encoding the novel amino acid sequences are changed via site-directed mutagenesis. This method uses oligonucleotide sequences to alter a polynucleotide to encode the desired amino acid variant, as well as sufficient adjacent nucleotides on both sides of the changed amino acid to form a stable duplex on either side of the site of being changed. In general, the techniques of site-directed mutagenesis are well known to those of skill in the art and this technique is exemplified by publications such as, Edelman et al., *DNA* 2:183 (1983). A versatile and efficient method for producing site-specific changes in a polynucleotide sequence was published by Zoller and Smith, *Nucleic Acids Res.* 10:6487-6500 (1982). PCR may also be used to create amino acid sequence variants of the novel nucleic acids. When small amounts of template DNA are used as starting material, primer(s) that differs slightly in sequence from the corresponding region in the template DNA can generate the desired amino acid variant. PCR amplification results in a population of product DNA fragments that differ from the polynucleotide template encoding the polypeptide at the position specified by the primer. The product DNA fragments replace the corresponding region in the plasmid and this gives a polynucleotide encoding the desired amino acid variant.

A further technique for generating amino acid variants is the cassette mutagenesis technique described in Wells et al., *Gene* 34:315 (1985); and other mutagenesis techniques well known in the art, such as, for example, the techniques in Sambrook et al., supra, and *Current Protocols in Molecular Biology*, Ausubel et al. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be used in the practice of the invention for the cloning and expression of these novel nucleic acids. Such DNA sequences include those which are capable of hybridizing to the appropriate novel nucleic acid sequence under stringent conditions.

Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA, amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

In accordance with the invention, polynucleotide sequences comprising the mature protein coding sequences corresponding to any one of SEQ ID NO:1-739, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et al. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, e.g., plasmids, cosmids, lambda phage derivatives, phagemids, and the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the invention and a host cell containing the polynucleotide.

In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell. Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be a prokaryotic or eukaryotic cell and can be a unicellular organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NO:1-739 or a fragment thereof or any other polynucleotides of the invention. In one embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a nucleic acid having any of the nucleotide sequences of SEQ ID NO:1-739 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and promoters are known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example. Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia). Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, *e.g.*, the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly-expressed gene to direct transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired characteristics, *e.g.*, stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination signals in operable reading phase with a functional promoter. The vector will comprise one or more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for transformation include *E. coli*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example,

pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced or derepressed by appropriate means (*e.g.*, temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

4.3 ANTISENSE

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1-739, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID NO:740-1478 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO:1-739 are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence of the invention. The term "coding

region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding a nucleic acid disclosed herein (*e.g.*, SEQ ID NO:1-739 , antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of a mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of a mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of a mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine,

pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a protein according to the invention to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res* 15: 6625-6641). The antisense nucleic acid molecule can also comprise a

2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res* 15: 6131-6148) or a chimeric RNA -DNA analogue (Inoue *et al.* (1987) *FEBS Lett* 215: 327-330).

4.4 RIBOZYMES AND PNA MOIETIES

In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as a mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave a mRNA transcripts to thereby inhibit translation of a mRNA. A ribozyme having specificity for a nucleic acid of the invention can be designed based upon the nucleotide sequence of a DNA disclosed herein (*i.e.*, SEQ ID NO:1-739). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a SECX-encoding mRNA. See, *e.g.*, Cech *et al.* U.S. Pat. No. 4,987,071; and Cech *et al.* U.S. Pat. No. 5,116,742. Alternatively, SECX mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region (*e.g.*, promoter and/or enhancers) to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene. (1991) *Anticancer Drug Des.* 6: 569-84; Helene. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14: 807-15.

In various embodiments, the nucleic acids of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.* (1996) *Bioorg Med Chem* 4: 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to

allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996) above; Perry-O'Keefe *et al.* (1996) *PNAS* 93: 14670-675.

PNAs of the invention can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of the invention can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup B. (1996) above); or as probes or primers for DNA sequence and hybridization (Hyrup *et al.* (1996), above; Perry-O'Keefe (1996), above).

In another embodiment, PNAs of the invention can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated that may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) above). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) above and Finn *et al.* (1996) *Nucl Acids Res* 24: 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag *et al.* (1989) *Nucl Acid Res* 17: 5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.* (1996) above). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. See, Petersen *et al.* (1975) *Bioorg Med Chem Lett* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre *et al.*, 1987, Proc. *Natl. Acad. Sci.* 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (See, *e.g.*, Krol *et al.*, 1988, *BioTechniques* 6:958-976) or intercalating agents. (See, *e.g.*, Zon, 1988, *Pharm. Res.* 5: 539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, etc.

4.5 HOSTS

The present invention further provides host cells genetically engineered to contain the polynucleotides of the invention. For example, such host cells may contain nucleic acids of the invention introduced into the host cell using known transformation, transfection or infection methods. The present invention still further provides host cells genetically engineered to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell.

Knowledge of nucleic acid sequences allows for modification of cells to permit, or increase, expression of endogenous polypeptide. Cells can be modified (e.g., by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the polypeptide at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the encoding sequences. See, for example, PCT International Publication No. WO94/12650, PCT International Publication No. WO92/20808, and PCT International Publication No. WO91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (e.g., ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If

linked to the coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the recombinant construct into the host cell can be effected by calcium phosphate transfection, DEAE, dextran mediated transfection, or electroporation (Davis, L. et al., *Basic Methods in Molecular Biology* (1986)). The host cells containing one of the polynucleotides of the invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, Cv-1 cell, COS cells, 293 cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level. Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., in Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, Cell 23:175 (1981). Other cell lines capable of expressing a compatible vector are, for example, the C127, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells. Mammalian expression vectors will comprise an origin of replication, a

suitable promoter and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5′ flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements. Recombinant polypeptides and proteins produced in bacterial culture are usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or insects or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli, Bacillus subtilis, Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations

of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequence include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the host cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.6 POLYPEPTIDES OF THE INVENTION

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising: the amino acid sequences set forth as any one of SEQ ID NO:740-1478 or an amino acid sequence encoded by any one of the nucleotide sequences SEQ ID NO:1-739 or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides preferably with biological or immunological activity that are encoded by: (a) a polynucleotide having any one of the nucleotide sequences set forth in SEQ ID NO:1-739 or (b) polynucleotides encoding any one of the amino acid sequences set forth as SEQ ID NO:740-1478 or (c) polynucleotides that hybridize to the complement of the polynucleotides of either (a) or (b) under stringent hybridization conditions. The invention also provides biologically active or immunologically active variants of any of the amino acid sequences set forth as SEQ ID NO:740-1478 or the corresponding full length or mature protein; and "substantial equivalents" thereof (e.g., with at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, typically at least about 95%, more typically at least about 98%, or most typically at least about 99% amino acid identity) that retain biological activity. Polypeptides encoded by allelic variants may have a similar, increased, or decreased activity compared to polypeptides comprising SEQ ID NO:740-1478.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H. U. Saragovi, et al., Bio/Technology 10, 773-778 (1992) and in R. S. McDowell, et al., J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites.

The present invention also provides both full-length and mature forms (for example, without a signal sequence or precursor sequence) of the disclosed proteins. The protein coding sequence is identified in the sequence listing by translation of the

disclosed nucleotide sequences. The mature form of such protein may be obtained by expression of a full-length polynucleotide in a suitable mammalian cell or other host cell. The sequence of the mature form of the protein is also determinable from the amino acid sequence of the full-length form. Where proteins of the present invention are membrane bound, soluble forms of the proteins are also provided. In such forms, part or all of the regions causing the proteins to be membrane bound are deleted so that the proteins are fully secreted from the cell in which they are expressed.

Protein compositions of the present invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (*e.g.*, an ORF) by nucleotide sequence but, due to the degeneracy of the genetic code, encode an identical polypeptide sequence. Preferred nucleic acid fragments of the present invention are the ORFs that encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. This technique is particularly useful in producing small peptides and fragments of larger polypeptides. Fragments are useful, for example, in generating antibodies against the native polypeptide. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The polypeptides and proteins of the present invention can alternatively be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein

which it normally does not produce or which the cell normally produces at a lower level. One skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

The invention also relates to methods for producing a polypeptide comprising growing a culture of host cells of the invention in a suitable culture medium, and purifying the protein from the cells or the culture in which the cells are grown. For example, the methods of the invention include a process for producing a polypeptide in which a host cell containing a suitable expression vector that includes a polynucleotide of the invention is cultured under conditions that allow expression of the encoded polypeptide. The polypeptide can be recovered from the culture, conveniently from the culture medium, or from a lysate prepared from the host cells and further purified. Preferred embodiments include those in which the protein produced by such process is a full length or mature form of the protein.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily follow known methods for isolating polypeptides and proteins in order to obtain one of the isolated polypeptides or proteins of the present invention. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography. See, *e.g.*, Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag (1994); Sambrook, et al., in Molecular Cloning: *A Laboratory Manual*; Ausubel et al., *Current Protocols in Molecular Biology*. Polypeptide fragments that retain biological/immunological activity include fragments comprising greater than about 100 amino acids, or greater than about 200 amino acids, and fragments that encode specific protein domains.

The purified polypeptides can be used in *in vitro* binding assays which are well known in the art to identify molecules which bind to the polypeptides. These molecules include but are not limited to, for e.g., small molecules, molecules from combinatorial libraries, antibodies or other proteins. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models

that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

In addition, the peptides of the invention or molecules capable of binding to the peptides may be complexed with toxins, e.g., ricin or cholera, or with other compounds that are toxic to cells. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for SEQ ID NO:740-1478.

The protein of the invention may also be expressed as a product of transgenic animals, *e.g.*, as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications, in the peptide or DNA sequence, can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, *e.g.*, U.S. Pat. No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein. Regions of the protein that are important for the protein function can be determined by various methods known in the art including the alanine-scanning method which involved systematic substitution of single or strings of amino acids with alanine, followed by testing the resulting alanine-containing variant for biological activity. This type of analysis determines the importance of the substituted amino acid(s) in biological activity. Regions of the protein that are important for protein function may be determined by the eMATRIX program.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and are useful for screening or other

immunological methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are encompassed by the present invention.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, *e.g.*, Invitrogen, San Diego, Calif., U.S.A. (the MaxBat™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (*i.e.*, from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl™ or Cibacrom blue 3GA Sepharose™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX), or as a His tag. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and Invitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("FLAG®") is commercially available from Kodak (New Haven, Conn.).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, *e.g.*, silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The polypeptides of the invention include analogs (variants). This embraces fragments, as well as peptides in which one or more amino acids has been deleted, inserted, or substituted. Also, analogs of the polypeptides of the invention embrace fusions of the polypeptides or modifications of the polypeptides of the invention, wherein the polypeptide or analog is fused to another moiety or moieties, e.g., targeting moiety or another therapeutic agent. Such analogs may exhibit improved properties such as activity and/or stability. Examples of moieties which may be fused to the polypeptide or an analog include, for example, targeting moieties which provide for the delivery of polypeptide to pancreatic cells, e.g., antibodies to pancreatic cells, antibodies to immune cells such as T-cells, monocytes, dendritic cells, granulocytes, etc., as well as receptor and ligands expressed on pancreatic or immune cells. Other moieties which may be fused to the polypeptide include therapeutic agents which are used for treatment, for example, immunosuppressive drugs such as cyclosporin, SK506, azathioprine, CD3 antibodies and steroids. Also, polypeptides may be fused to immune modulators, and other cytokines such as alpha or beta interferon.

4.6.1 DETERMINING POLYPEPTIDE AND POLYNUCLEOTIDE IDENTITY AND SIMILARITY

Preferred identity and/or similarity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs including, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., Nucleic Acids Research 12(1):387 (1984); Genetics Computer Group, University of Wisconsin, Madison, WI), BLASTP, BLASTN, BLASTX, FASTA (Altschul, S.F. et al., J. Molec. Biol. 215:403-410 (1990), PSI-BLAST

(Altschul S.F. et al., Nucleic Acids Res. vol. 25, pp. 3389-3402, herein incorporated by reference), eMatrix software (Wu et al., J. Comp. Biol., Vol. 6, pp. 219-235 (1999), herein incorporated by reference), eMotif software (Nevill-Manning et al, ISMB-97, Vol. 4, pp. 202-209, herein incorporated by reference), pFam software (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1), pp. 320-322 (1998), herein incorporated by reference) and the Kyte-Doolittle hydrophobocity prediction algorithm (J. Mol Biol, 157, pp. 105-31 (1982), incorporated herein by reference). The BLAST programs are publicly available from the National Center for Biotechnology Information (NCBI) and other sources (BLAST Manual, Altschul, S., et al. NCB NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990).

4.7 CHIMERIC AND FUSION PROTEINS

The invention also provides chimeric or fusion proteins. As used herein, a "chimeric protein" or "fusion protein" comprises a polypeptide of the invention operatively linked to another polypeptide. Within a fusion protein the polypeptide according to the invention can correspond to all or a portion of a protein according to the invention. In one embodiment, a fusion protein comprises at least one biologically active portion of a protein according to the invention. In another embodiment, a fusion protein comprises at least two biologically active portions of a protein according to the invention. Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide according to the invention and the other polypeptide are fused in-frame to each other. The polypeptide can be fused to the N-terminus or C-terminus.

For example, in one embodiment a fusion protein comprises a polypeptide according to the invention operably linked to the extracellular domain of a second protein.

In another embodiment, the fusion protein is a GST-fusion protein in which the polypeptide sequences of the invention are fused to the C-terminus of the GST (i.e., glutathione S-transferase) sequences.

In another embodiment, the fusion protein is an immunoglobulin fusion protein in which the polypeptide sequences according to the invention comprises one or more domains are fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into

pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand and a protein of the invention on the surface of a cell, to thereby suppress signal transduction *in vivo*. The immunoglobulin fusion proteins can be used to affect the bioavailability of a cognate ligand. Inhibition of the ligand/protein interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, *e,g.*, cancer as well as modulating (*e.g.*, promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies in a subject, to purify ligands, and in screening assays to identify molecules that inhibit the interaction of a polypeptide of the invention with a ligand.

A chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for example, Ausubel et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protein of the invention.

4.8 GENE THERAPY

Mutations in the polynucleotides of the invention gene may result in loss of normal function of the encoded protein. The invention thus provides gene therapy to restore normal activity of the polypeptides of the invention; or to treat disease states

involving polypeptides of the invention. Delivery of a functional gene encoding polypeptides of the invention to appropriate cells is effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (e.g., adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (e.g., liposomes or chemical treatments). See, for example, Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, Science, 244: 1275-1281 (1989); Verma, Scientific American: 68-84 (1990); and Miller, Nature, 357: 455-460 (1992). Introduction of any one of the nucleotides of the present invention or a gene encoding the polypeptides of the present invention can also be accomplished with extrachromosomal substrates (transient expression) or artificial chromosomes (stable expression). Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes. Alternatively, it is contemplated that in other human disease states, preventing the expression of or inhibiting the activity of polypeptides of the invention will be useful in treating the disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of polypeptides of the invention.

Other methods inhibiting expression of a protein include the introduction of antisense molecules to the nucleic acids of the present invention, their complements, or their translated RNA sequences, by methods known in the art. Further, the polypeptides of the present invention can be inhibited by using targeted deletion methods, or the insertion of a negative regulatory element such as a silencer, which is tissue specific.

The present invention still further provides cells genetically engineered *in vivo* to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell. These methods can be used to increase or decrease the expression of the polynucleotides of the present invention.

Knowledge of DNA sequences provided by the invention allows for modification of cells to permit, increase, or decrease, expression of endogenous polypeptide. Cells can be modified (e.g., by homologous recombination) to provide increased polypeptide expression

by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the protein at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the desired protein encoding sequences. See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and PCT International Publication No. WO 91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (e.g., ada, dhfr, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the desired protein coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a

tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

4.9 TRANSGENIC ANIMALS

In preferred methods to determine biological functions of the polypeptides of the invention in vivo, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in

disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of a promoter of the polynucleotides of the invention is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

The polynucleotides of the present invention also make possible the development, through, e.g., homologous recombination or knock out strategies, of animals that fail to express polypeptides of the invention or that express a variant polypeptide. Such animals are useful as models for studying the *in vivo* activities of polypeptide as well as for studying modulators of the polypeptides of the invention.

In preferred methods to determine biological functions of the polypeptides of the invention *in vivo*, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of the polynucleotides of the invention promoter is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

4.10 USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified herein. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA). The mechanism underlying the particular condition or pathology will dictate whether the polypeptides of the invention, the polynucleotides of the invention or modulators (activators or inhibitors) thereof would be beneficial to the subject in need of treatment. Thus, "therapeutic compositions of the invention" include compositions comprising isolated polynucleotides (including recombinant DNA molecules, cloned genes and degenerate variants thereof) or polypeptides of the invention (including full length protein, mature protein and truncations or domains thereof), or compounds and other substances that modulate the overall activity of the target gene products, either at the level of target gene/protein expression or target protein activity. Such modulators include polypeptides, analogs, (variants), including fragments and fusion proteins, antibodies and other binding proteins; chemical compounds that directly or indirectly activate or inhibit the polypeptides of the invention (identified, e.g., via drug screening assays as described herein); antisense polynucleotides and polynucleotides suitable for triple helix formation; and in particular antibodies or other binding partners that specifically recognize one or more epitopes of the polypeptides of the invention.

The polypeptides of the present invention may likewise be involved in cellular activation or in one of the other physiological pathways described herein.

4.10.1 RESEARCH USES AND UTILITIES

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding polypeptide is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of

course, to isolate correlative receptors or ligands. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or ago: of the binding interaction.

Any or all of these research utilities are capable of being developed into reagei grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled ir the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

4.10.2 NUTRITIONAL USES

Polynucleotides and polypeptides of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the polypeptide or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the polypeptide or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

4.10.3 CYTOKINE AND CELL PROLIFERATION/DIFFERENTIATION ACTIVITY

A polypeptide of the present invention may exhibit activity relating to cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of therapeutic

compositions of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+(preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e, CMK, HUVEC, and Caco. Therapeutic compositions of the invention can be used in the following:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., I. Immunol. 149:3778-3783, 1992; Bowman et al., I. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A. M. and Shevach, E. M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human interleukin-γ, Schreiber, R. D. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L. S. and Lipsky, P. E. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6--Nordan, R. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Aced. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11--Bennett, F., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.15.1 John

Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9--Ciarletta, A., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

4.10.4 STEM CELL GROWTH FACTOR ACTIVITY

A polypeptide of the present invention may exhibit stem cell growth factor activity and be involved in the proliferation, differentiation and survival of pluripotent and totipotent stem cells including primordial germ cells, embryonic stem cells, hematopoietic stem cells and/or germ line stem cells. Administration of the polypeptide of the invention to stem cells *in vivo* or *ex vivo* is expected to maintain and expand cell populations in a totipotential or pluripotential state which would be useful for re-engineering damaged or diseased tissues, transplantation, manufacture of bio-pharmaceuticals and the development of bio-sensors. The ability to produce large quantities of human cells has important working applications for the production of human proteins which currently must be obtained from non-human sources or donors, implantation of cells to treat diseases such as Parkinson's, Alzheimer's and other neurodegenerative diseases; tissues for grafting such as bone marrow, skin, cartilage, tendons, bone, muscle (including cardiac muscle), blood vessels, cornea, neural cells, gastrointestinal cells and others; and organs for transplantation such as kidney, liver, pancreas (including islet cells), heart and lung.

It is contemplated that multiple different exogenous growth factors and/or cytokines may be administered in combination with the polypeptide of the invention to achieve the desired effect, including any of the growth factors listed herein, other stem cell maintenance factors, and specifically including stem cell factor (SCF), leukemia inhibitory factor (LIF), Flt-3 ligand (Flt-3L), any of the interleukins, recombinant soluble IL-6 receptor fused to IL-6, macrophage inflammatory protein 1-alpha (MIP-1-alpha), G-CSF, GM-CSF, thrombopoietin (TPO), platelet factor 4 (PF-4), platelet-derived growth factor (PDGF), neural growth factors and basic fibroblast growth factor (bFGF).

Since totipotent stem cells can give rise to virtually any mature cell type, expansion of these cells in culture will facilitate the production of large quantities of mature cells. Techniques for culturing stem cells are known in the art and administration of polypeptides of the invention, optionally with other growth factors and/or cytokines, is expected to enhance the survival and proliferation of the stem cell populations. This can be accomplished by direct administration of the polypeptide of the invention to the culture medium. Alternatively, stroma cells transfected with a polynucleotide that encodes for the polypeptide of the invention can be used as a feeder layer for the stem cell populations in culture or in vivo. Stromal support cells for feeder layers may include embryonic bone marrow fibroblasts, bone marrow stromal cells, fetal liver cells, or cultured embryonic fibroblasts (see U.S. Patent No. 5,690,926).

Stem cells themselves can be transfected with a polynucleotide of the invention to induce autocrine expression of the polypeptide of the invention. This will allow for generation of undifferentiated totipotential/pluripotential stem cell lines that are useful as is or that can then be differentiated into the desired mature cell types. These stable cell lines can also serve as a source of undifferentiated totipotential/pluripotential mRNA to create cDNA libraries and templates for polymerase chain reaction experiments. These studies would allow for the isolation and identification of differentially expressed genes in stem cell populations that regulate stem cell proliferation and/or maintenance.

Expansion and maintenance of totipotent stem cell populations will be useful in the treatment of many pathological conditions. For example, polypeptides of the present invention may be used to manipulate stem cells in culture to give rise to neuroepithelial cells that can be used to augment or replace cells damaged by illness, autoimmune

disease, accidental damage or genetic disorders. The polypeptide of the invention may be useful for inducing the proliferation of neural cells and for the regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders which involve degeneration, death or trauma to neural cells or nerve tissue. In addition, the expanded stem cell populations can also be genetically altered for gene therapy purposes and to decrease host rejection of replacement tissues after grafting or implantation.

Expression of the polypeptide of the invention and its effect on stem cells can also be manipulated to achieve controlled differentiation of the stem cells into more differentiated cell types. A broadly applicable method of obtaining pure populations of a specific differentiated cell type from undifferentiated stem cell populations involves the use of a cell-type specific promoter driving a selectable marker. The selectable marker allows only cells of the desired type to survive. For example, stem cells can be induced to differentiate into cardiomyocytes (Wobus et al., Differentiation, 48: 173-182, (1991); Klug et al., J. Clin. Invest., 98(1): 216-224, (1998)) or skeletal muscle cells (Browder, L. W. In: *Principles of Tissue Engineering eds.* Lanza et al., Academic Press (1997)). Alternatively, directed differentiation of stem cells can be accomplished by culturing the stem cells in the presence of a differentiation factor such as retinoic acid and an antagonist of the polypeptide of the invention which would inhibit the effects of endogenous stem cell factor activity and allow differentiation to proceed.

In vitro cultures of stem cells can be used to determine if the polypeptide of the invention exhibits stem cell growth factor activity. Stem cells are isolated from any one of various cell sources (including hematopoietic stem cells and embryonic stem cells) and cultured on a feeder layer, as described by Thompson et al. Proc. Natl. Acad. Sci, U.S.A., 92: 7844-7848 (1995), in the presence of the polypeptide of the invention alone or in combination with other growth factors or cytokines. The ability of the polypeptide of the invention to induce stem cells proliferation is determined by colony formation on semi-solid support e.g. as described by Bernstein et al., Blood, 77: 2316-2321 (1991).

4.10.5 HEMATOPOIESIS REGULATING ACTIVITY

A polypeptide of the present invention may be involved in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell disorders. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

Therapeutic compositions of the invention can be used in the following:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M. G. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, N.Y. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I. K. and Briddell, R. A. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, N.Y. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R. E. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, N.Y. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, N.Y. 1994; Long term culture initiating cell assay, Sutherland, H. J. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, N.Y. 1994.

4.10.6 TISSUE GROWTH ACTIVITY

A polypeptide of the present invention also may be involved in bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as in wound healing and tissue repair and replacement, and in healing of burns, incisions and ulcers.

A polypeptide of the present invention which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Compositions of a polypeptide, antibody, binding partner, or other modulator of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A polypeptide of this invention may also be involved in attracting bone-forming cells, stimulating growth of bone-forming cells, or inducing differentiation of progenitors of bone-forming cells. Treatment of osteoporosis, osteoarthritis, bone degenerative

disorders, or periodontal disease, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes may also be possible using the composition of the invention.

Another category of tissue regeneration activity that may involve the polypeptide of the present invention is tendon/ligament formation. Induction of tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The compositions of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a composition may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager

syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a composition of the invention.

Compositions of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

Compositions of the present invention may also be involved in the generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring may allow normal tissue to regenerate. A polypeptide of the present invention may also exhibit angiogenic activity.

A composition of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A composition of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Therapeutic compositions of the invention can be used in the following:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, H. I. and Rovee, D. T., eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

4.10.7 IMMUNE STIMULATING OR SUPPRESSING ACTIVITY

A polypeptide of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A polynucleotide of the invention can encode a polypeptide exhibiting such activities. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpes viruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, proteins of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein (or antagonists thereof, including antibodies) of the present invention may also to be useful in the treatment of allergic reactions and conditions (*e.g.*, anaphylaxis, serum sickness, drug reactions, food allergies, insect venom allergies, mastocytosis, allergic rhinitis, hypersensitivity pneumonitis, urticaria, angioedema, eczema, atopic dermatitis, allergic contact dermatitis, erythema multiforme, Stevens-Johnson syndrome, allergic conjunctivitis, atopic keratoconjunctivitis, venereal keratoconjunctivitis, giant papillary conjunctivitis and contact allergies), such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein (or antagonists thereof) of the present invention. The therapeutic effects of the

polypeptides or antagonists thereof on allergic reactions can be evaluated by in vivo animals models such as the cumulative contact enhancement test (Lastbom et al., Toxicology 125: 59-66, 1998), skin prick test (Hoffmann et al., Allergy 54: 446-54, 1999), guinea pig skin sensitization test (Vohr et al., Arch. Toxocol. 73: 501-9), and murine local lymph node assay (Kimber et al., J. Toxicol. Environ. Health 53: 563-79).

Using the proteins of the invention it may also be possible to modulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a therapeutic composition of the invention may prevent cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, a lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a

subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular therapeutic compositions in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of therapeutic compositions of the invention on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block stimulation of T cells can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (e.g., a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or

eliciting an initial immune response. For example, enhancing an immune response may be useful in cases of viral infection, including systemic viral diseases such as influenza, the common cold, and encephalitis.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

A polypeptide of the present invention may provide the necessary stimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I alpha chain protein and β_2 microglobulin protein or an MHC class II alpha chain protein and an MHC class II beta chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., I. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bowman et al., J. Virology 61:1992-1998; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J. J. and Brunswick, M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology

154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

4.10.8 ACTIVIN/INHIBIN ACTIVITY

A polypeptide of the present invention may also exhibit activin- or inhibin-related activities. A polynucleotide of the invention may encode a polypeptide exhibiting such characteristics. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a polypeptide of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, U.S. Pat. No. 4,798,885. A polypeptide of the invention may

also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as, but not limited to, cows, sheep and pigs.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods.

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

4.10.9 CHEMOTACTIC/CHEMOKINETIC ACTIVITY

A polypeptide of the present invention may be involved in chemotactic or chemokinetic activity for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Chemotactic and chemokinetic receptor activation can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic compositions (e.g. proteins, antibodies, binding partners, or modulators of the invention) provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

Therapeutic compositions of the invention can be used in the following:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the

migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

4.10.10 HEMOSTATIC AND THROMBOLYTIC ACTIVITY

A polypeptide of the invention may also be involved in hemostatis or thrombolysis or thrombosis. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Compositions may be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A composition of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

Therapeutic compositions of the invention can be used in the following:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

4.10.11 CANCER DIAGNOSIS AND THERAPY

Polypeptides of the invention may be involved in cancer cell generation, proliferation or metastasis. Detection of the presence or amount of polynucleotides or polypeptides of the invention may be useful for the diagnosis and/or prognosis of one or more types of cancer. For example, the presence or increased expression of a

polynucleotide/polypeptide of the invention may indicate a hereditary risk of cancer, a precancerous condition, or an ongoing malignancy. Conversely, a defect in the gene or absence of the polypeptide may be associated with a cancer condition. Identification of single nucleotide polymorphisms associated with cancer or a predisposition to cancer may also be useful for diagnosis or prognosis.

Cancer treatments promote tumor regression by inhibiting tumor cell proliferation, inhibiting angiogenesis (growth of new blood vessels that is necessary to support tumor growth) and/or prohibiting metastasis by reducing tumor cell motility or invasiveness. Therapeutic compositions of the invention may be effective in adult and pediatric oncology including in solid phase tumors/malignancies, locally advanced tumors, human soft tissue sarcomas, metastatic cancer, including lymphatic metastases, blood cell malignancies including multiple myeloma, acute and chronic leukemias, and lymphomas, head and neck cancers including mouth cancer, larynx cancer and thyroid cancer, lung cancers including small cell carcinoma and non-small cell cancers, breast cancers including small cell carcinoma and ductal carcinoma, gastrointestinal cancers including esophageal cancer, stomach cancer, colon cancer, colorectal cancer and polyps associated with colorectal neoplasia, pancreatic cancers, liver cancer, urologic cancers including bladder cancer and prostate cancer, malignancies of the female genital tract including ovarian carcinoma, uterine (including endometrial) cancers, and solid tumor in the ovarian follicle, kidney cancers including renal cell carcinoma, brain cancers including intrinsic brain tumors, neuroblastoma, astrocytic brain tumors, gliomas, metastatic tumor cell invasion in the central nervous system, bone cancers including osteomas, skin cancers including malignant melanoma, tumor progression of human skin keratinocytes, squamous cell carcinoma, basal cell carcinoma, hemangiopericytoma and Karposi's sarcoma.

Polypeptides, polynucleotides, or modulators of polypeptides of the invention (including inhibitors and stimulators of the biological activity of the polypeptide of the invention) may be administered to treat cancer. Therapeutic compositions can be administered in therapeutically effective dosages alone or in combination with adjuvant cancer therapy such as surgery, chemotherapy, radiotherapy, thermotherapy, and laser therapy, and may provide a beneficial effect, e.g. reducing tumor size, slowing rate of

tumor growth, inhibiting metastasis, or otherwise improving overall clinical condition, without necessarily eradicating the cancer.

The composition can also be administered in therapeutically effective amounts as a portion of an anti-cancer cocktail. An anti-cancer cocktail is a mixture of the polypeptide or modulator of the invention with one or more anti-cancer drugs in addition to a pharmaceutically acceptable carrier for delivery. The use of anti-cancer cocktails as a cancer treatment is routine. Anti-cancer drugs that are well known in the art and can be used as a treatment in combination with the polypeptide or modulator of the invention include: Actinomycin D, Aminoglutethimide, Asparaginase, Bleomycin, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin (cis-DDP), Cyclophosphamide, Cytarabine HCl (Cytosine arabinoside), Dacarbazine, Dactinomycin, Daunorubicin HCl, Doxorubicin HCl, Estramustine phosphate sodium, Etoposide (V16-213), Floxuridine, 5-Fluorouracil (5-Fu), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leuprolide acetate (LHRH-releasing factor analog), Lomustine, Mechlorethamine HCl (nitrogen mustard), Melphalan, Mercaptopurine, Mesna, Methotrexate (MTX), Mitomycin, Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine sulfate, Vincristine sulfate, Amsacrine, Azacitidine, Hexamethylmelamine, Interleukin-2, Mitoguazone, Pentostatin, Semustine, Teniposide, and Vindesine sulfate.

In addition, therapeutic compositions of the invention may be used for prophylactic treatment of cancer. There are hereditary conditions and/or environmental situations (e.g. exposure to carcinogens) known in the art that predispose an individual to developing cancers. Under these circumstances, it may be beneficial to treat these individuals with therapeutically effective doses of the polypeptide of the invention to reduce the risk of developing cancers.

In vitro models can be used to determine the effective doses of the polypeptide of the invention as a potential cancer treatment. These *in vitro* models include proliferation assays of cultured tumor cells, growth of cultured tumor cells in soft agar (see Freshney, (1987) Culture of Animal Cells: A Manual of Basic Technique, Wily-Liss, New York, NY Ch 18 and Ch 21), tumor systems in nude mice as described in Giovanella et al., J. Natl. Can. Inst., 52: 921-30 (1974), mobility and invasive potential of tumor cells in

Boyden Chamber assays as described in Pilkington et al., Anticancer Res., 17: 4107-9 (1997), and angiogenesis assays such as induction of vascularization of the chick chorioallantoic membrane or induction of vascular endothelial cell migration as described in Ribatta et al., Intl. J. Dev. Biol., 40: 1189-97 (1999) and Li et al., Clin. Exp. Metastasis, 17:423-9 (1999), respectively. Suitable tumor cells lines are available, e.g. from American Type Tissue Culture Collection catalogs.

4.10.12 RECEPTOR/LIGAND ACTIVITY

A polypeptide of the present invention may also demonstrate activity as receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions. A polynucleotide of the invention can encode a polypeptide exhibiting such characteristics. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses. Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a polypeptide of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley- Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1- 7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

By way of example, the polypeptides of the invention may be used as a receptor for a ligand(s) thereby transmitting the biological activity of that ligand(s). Ligands may be identified through binding assays, affinity chromatography, dihybrid screening assays, BIAcore assays, gel overlay assays, or other methods known in the art.

Studies characterizing drugs or proteins as agonist or antagonist or partial agonists or a partial antagonist require the use of other proteins as competing ligands. The polypeptides of the present invention or ligand(s) thereof may be labeled by being coupled to radioisotopes, colorimetric molecules or a toxin molecules by conventional methods. ("Guide to Protein Purification" Murray P. Deutscher (ed) Methods in Enzymology Vol. 182 (1990) Academic Press, Inc. San Diego). Examples of radioisotopes include, but are not limited to, tritium and carbon-14 . Examples of colorimetric molecules include, but are not limited to, fluorescent molecules such as fluorescamine, or rhodamine or other colorimetric molecules. Examples of toxins include, but are not limited, to ricin.

4.10.13 DRUG SCREENING

This invention is particularly useful for screening chemical compounds by using the novel polypeptides or binding fragments thereof in any of a variety of drug screening techniques. The polypeptides or fragments employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or a fragment thereof. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between polypeptides of the invention or fragments and the agent being tested or examine the diminution in complex formation between the novel polypeptides and an appropriate cell line, which are well known in the art.

Sources for test compounds that may be screened for ability to bind to or modulate (i.e., increase or decrease) the activity of polypeptides of the invention include (1) inorganic and organic chemical libraries, (2) natural product libraries, and (3)

combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules.

Chemical libraries may be readily synthesized or purchased from a number of commercial sources, and may include structural analogs of known compounds or compounds that are identified as "hits" or "leads" via natural product screening.

The sources of natural product libraries are microorganisms (including bacteria and fungi), animals, plants or other vegetation, or marine organisms, and libraries of mixtures for screening may be created by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of the organisms themselves. Natural product libraries include polyketides, non-ribosomal peptides, and (non-naturally occurring) variants thereof. For a review, see *Science 282*:63-68 (1998).

Combinatorial libraries are composed of large numbers of peptides, oligonucleotides or organic compounds and can be readily prepared by traditional automated synthesis methods, PCR, cloning or proprietary synthetic methods. Of particular interest are peptide and oligonucleotide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, *Curr. Opin. Biotechnol.* 8:701-707 (1997). For reviews and examples of peptidomimetic libraries, see Al-Obeidi et al., *Mol. Biotechnol*, 9(3):205-23 (1998); Hruby et al., *Curr Opin Chem Biol*, 1(1):114-19 (1997); Dorner et al., *Bioorg Med Chem*, 4(5):709-15 (1996) (alkylated dipeptides).

Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to bind a polypeptide of the invention. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

The binding molecules thus identified may be complexed with toxins, e.g., ricin or cholera, or with other compounds that are toxic to cells such as radioisotopes. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity

of the binding molecule for a polypeptide of the invention. Alternatively, the binding molecules may be complexed with imaging agents for targeting and imaging purposes.

4.10.14 ASSAY FOR RECEPTOR ACTIVITY

The invention also provides methods to detect specific binding of a polypeptide e.g. a ligand or a receptor. The art provides numerous assays particularly useful for identifying previously unknown binding partners for receptor polypeptides of the invention. For example, expression cloning using mammalian or bacterial cells, or dihybrid screening assays can be used to identify polynucleotides encoding binding partners. As another example, affinity chromatography with the appropriate immobilized polypeptide of the invention can be used to isolate polypeptides that recognize and bind polypeptides of the invention. There are a number of different libraries used for the identification of compounds, and in particular small molecules, that modulate (*i.e.*, increase or decrease) biological activity of a polypeptide of the invention. Ligands for receptor polypeptides of the invention can also be identified by adding exogenous ligands, or cocktails of ligands to two cells populations that are genetically identical except for the expression of the receptor of the invention: one cell population expresses the receptor of the invention whereas the other does not. The response of the two cell populations to the addition of ligands(s) are then compared. Alternatively, an expression library can be co-expressed with the polypeptide of the invention in cells and assayed for an autocrine response to identify potential ligand(s). As still another example, BIAcore assays, gel overlay assays, or other methods known in the art can be used to identify binding partner polypeptides, including, (1) organic and inorganic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules.

The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined. For example, a chimeric protein in which the cytoplasmic domain of the polypeptide of the invention is fused to the extracellular portion of a protein, whose ligand has been identified, is produced in a host cell. The cell is then incubated with the ligand specific for the extracellular portion of the chimeric protein, thereby activating the chimeric receptor. Known downstream proteins

involved in intracellular signaling can then be assayed for expected modifications i.e. phosphorylation. Other methods known to those in the art can also be used to identify signaling molecules involved in receptor activity.

4.10.15 ANTI-INFLAMMATORY ACTIVITY

Compositions of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Compositions with such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation intimation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Compositions of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Compositions of this invention may be utilized to prevent or treat conditions such as, but not limited to, sepsis, acute pancreatitis, endotoxin shock, cytokine induced shock, rheumatoid arthritis, chronic inflammatory arthritis, pancreatic cell damage from diabetes mellitus type 1, graft versus host disease, inflammatory bowel disease, inflamation associated with pulmonary disease, other autoimmune disease or inflammatory disease, an antiproliferative agent such as for acute or chronic mylegenous leukemia or in the prevention of premature labor secondary to intrauterine infections.

4.10.16 LEUKEMIAS

Leukemias and related disorders may be treated or prevented by administration of a therapeutic that promotes or inhibits function of the polynucleotides and/or polypeptides of the invention. Such leukemias and related disorders include but are not

limited to acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia, chronic leukemia, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia (for a review of such disorders, see Fishman et al., 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia).

4.10.17 NERVOUS SYSTEM DISORDERS

Nervous system disorders, involving cell types which can be tested for efficacy of intervention with compounds that modulate the activity of the polynucleotides and/or polypeptides of the invention, and which can be treated upon thus observing an indication of therapeutic utility, include but are not limited to nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the invention include but are not limited to the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems:

(i) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions which sever a portion of the nervous system, or compression injuries;

(ii) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia;

(iii) infectious lesions, in which a portion of the nervous system is destroyed or injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, syphilis;

(iv) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to degeneration associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis;

(v) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration;

(vi) neurological lesions associated with systemic diseases including but not limited to diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;

(vii) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and

(viii) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including but not limited to multiple sclerosis, human immunodeficiency virus-associated myelopathy, transverse myelopathy or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

Therapeutics which are useful according to the invention for treatment of a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, therapeutics which elicit any of the following effects may be useful according to the invention:

(i) increased survival time of neurons in culture;

(ii) increased sprouting of neurons in culture or in vivo;

(iii) increased production of a neuron-associated molecule in culture or *in vivo*, *e.g.*, choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or

(iv) decreased symptoms of neuron dysfunction in vivo.

Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may be measured by the method set forth in Arakawa et al. (1990, J. Neurosci. 10:3507-3515); increased sprouting of neurons may be detected by methods set forth in Pestronk et al. (1980, Exp. Neurol. 70:65-82) or Brown et al. (1981, Ann. Rev. Neurosci. 4:17-42); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody

binding, Northern blot assay, *etc.*, depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, *e.g.*, weakness, motor neuron conduction velocity, or functional disability.

In specific embodiments, motor neuron disorders that may be treated according to the invention include but are not limited to disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including but not limited to progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).

4.10.18 OTHER ACTIVITIES

A polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, co-factors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related

diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

4.10.19 IDENTIFICATION OF POLYMORPHISMS

The demonstration of polymorphisms makes possible the identification of such polymorphisms in human subjects and the pharmacogenetic use of this information for diagnosis and treatment. Such polymorphisms may be associated with, e.g., differential predisposition or susceptibility to various disease states (such as disorders involving inflammation or immune response) or a differential response to drug administration, and this genetic information can be used to tailor preventive or therapeutic treatment appropriately. For example, the existence of a polymorphism associated with a predisposition to inflammation or autoimmune disease makes possible the diagnosis of this condition in humans by identifying the presence of the polymorphism.

Polymorphisms can be identified in a variety of ways known in the art which all generally involve obtaining a sample from a patient, analyzing DNA from the sample, optionally involving isolation or amplification of the DNA, and identifying the presence of the polymorphism in the DNA. For example, PCR may be used to amplify an appropriate fragment of genomic DNA which may then be sequenced. Alternatively, the DNA may be subjected to allele-specific oligonucleotide hybridization (in which appropriate oligonucleotides are hybridized to the DNA under conditions permitting detection of a single base mismatch) or to a single nucleotide extension assay (in which an oligonucleotide that hybridizes immediately adjacent to the position of the polymorphism is extended with one or more labeled nucleotides). In addition, traditional restriction fragment length polymorphism analysis (using restriction enzymes that provide differential digestion of the genomic DNA depending on the presence or absence of the polymorphism) may be performed. Arrays with nucleotide sequences of the present invention can be used to detect polymorphisms. The array can comprise modified nucleotide sequences of the present invention in order to detect the nucleotide sequences

of the present invention. In the alternative, any one of the nucleotide sequences of the present invention can be placed on the array to detect changes from those sequences.

Alternatively a polymorphism resulting in a change in the amino acid sequence could also be detected by detecting a corresponding change in amino acid sequence of the protein, e.g., by an antibody specific to the variant sequence.

4.10.20 ARTHRITIS AND INFLAMMATION

The immunosuppressive effects of the compositions of the invention against rheumatoid arthritis is determined in an experimental animal model system. The experimental model system is adjuvant induced arthritis in rats, and the protocol is described by J. Holoshitz, et at., 1983, Science, 219:56, or by B. Waksman et al., 1963, Int. Arch. Allergy Appl. Immunol., 23:129. Induction of the disease can be caused by a single injection, generally intradermally, of a suspension of killed Mycobacterium tuberculosis in complete Freund's adjuvant (CFA). The route of injection can vary, but rats may be injected at the base of the tail with an adjuvant mixture. The polypeptide is administered in phosphate buffered solution (PBS) at a dose of about 1-5 mg/kg. The control consists of administering PBS only.

The procedure for testing the effects of the test compound would consist of intradermally injecting killed Mycobacterium tuberculosis in CFA followed by immediately administering the test compound and subsequent treatment every other day until day 24. At 14, 15, 18, 20, 22, and 24 days after injection of Mycobacterium CFA, an overall arthritis score may be obtained as described by J. Holoskitz above. An analysis of the data would reveal that the test compound would have a dramatic affect on the swelling of the joints as measured by a decrease of the arthritis score.

4.11 THERAPEUTIC METHODS

The compositions (including polypeptide fragments, analogs, variants and antibodies or other binding partners or modulators including antisense polynucleotides) of the invention have numerous applications in a variety of therapeutic methods. Examples of therapeutic applications include, but are not limited to, those exemplified herein.

4.11.1 EXAMPLE

One embodiment of the invention is the administration of an effective amount of the polypeptides or other composition of the invention to individuals affected by a disease or disorder that can be modulated by regulating the peptides of the invention. While the mode of administration is not particularly important, parenteral administration is preferred. An exemplary mode of administration is to deliver an intravenous bolus. The dosage of the polypeptides or other composition of the invention will normally be determined by the prescribing physician. It is to be expected that the dosage will vary according to the age, weight, condition and response of the individual patient. Typically, the amount of polypeptide administered per dose will be in the range of about 0.01μg/kg to 100 mg/kg of body weight, with the preferred dose being about 0.1μg/kg to 10 mg/kg of patient body weight. For parenteral administration, polypeptides of the invention will be formulated in an injectable form combined with a pharmaceutically acceptable parenteral vehicle. Such vehicles are well known in the art and examples include water, saline, Ringer's solution, dextrose solution, and solutions consisting of small amounts of the human serum albumin. The vehicle may contain minor amounts of additives that maintain the isotonicity and stability of the polypeptide or other active ingredient. The preparation of such solutions is within the skill of the art.

4.12 PHARMACEUTICAL FORMULATIONS AND ROUTES OF ADMINISTRATION

A protein or other composition of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources and including antibodies and other binding partners of the polypeptides of the invention) may be administered to a patient in need, by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s) at doses to treat or ameliorate a variety of disorders. Such a composition may optionally contain (in addition to protein or other active ingredient and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity

of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the disease or disorder in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), insulin-like growth factor (IGF), as well as cytokines described herein.

The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or other active ingredient or complement its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein or other active ingredient of the invention, or to minimize side effects. Conversely, protein or other active ingredient of the present invention may be included in formulations of the particular clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti- inflammatory agent to minimize side effects of the clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent (such as IL-1Ra, IL-1 Hy1, IL-1 Hy2, anti-TNF, corticosteroids, immunosuppressive agents). A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

As an alternative to being included in a pharmaceutical composition of the invention including a first protein, a second protein or a therapeutic agent may be concurrently administered with the first protein (e.g., at the same time, or at differing times provided that therapeutic concentrations of the combination of agents is achieved at the treatment site). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition. A therapeutically effective dose further refers

to that amount of the compound sufficient to result in amelioration of symptoms, *e.g.*, treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein or other active ingredient of the present invention is administered to a mammal having a condition to be treated. Protein or other active ingredient of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein or other active ingredient of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein or other active ingredient of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

4.12.1 ROUTES OF ADMINISTRATION

Suitable routes of administration may, for example, include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Administration of protein or other active ingredient of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or

cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

Alternately, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into a arthritic joints or in fibrotic tissue, often in a depot or sustained release formulation. In order to prevent the scarring process frequently occurring as complication of glaucoma surgery, the compounds may be administered topically, for example, as eye drops. Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with a specific antibody, targeting, for example, arthritic or fibrotic tissue. The liposomes will be targeted to and taken up selectively by the afflicted tissue.

The polypeptides of the invention are administered by any route that delivers an effective dosage to the desired site of action. The determination of a suitable route of administration and an effective dosage for a particular indication is within the level of skill in the art. Preferably for wound treatment, one administers the therapeutic compound directly to the site. Suitable dosage ranges for the polypeptides of the invention can be extrapolated from these dosages or from similar studies in appropriate animal models. Dosages can then be adjusted as necessary by the clinician to provide maximal therapeutic benefit.

4.12.2 COMPOSITIONS/FORMULATIONS

Pharmaceutical compositions for use in accordance with the present invention thus may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. These pharmaceutical compositions may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Proper formulation is dependent upon the route of administration chosen. When a therapeutically effective amount of protein or other active ingredient of the present invention is administered orally, protein or other active ingredient of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the

pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein or other active ingredient of the present invention, and preferably from about 25 to 90% protein or other active ingredient of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein or other active ingredient of the present invention, and preferably from about 1 to 50% protein or other active ingredient of the present invention.

When a therapeutically effective amount of protein or other active ingredient of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein or other active ingredient of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein or other active ingredient solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein or other active ingredient of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art.

Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained from a solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for such administration. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon

dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, *e.g.*, gelatin for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch. The compounds may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, *e.g.*, containing conventional suppository bases such as cocoa butter or other glycerides. In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

A pharmaceutical carrier for the hydrophobic compounds of the invention is a co-solvent system comprising benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. The co-solvent system may be the VPD co-solvent system. VPD is a solution of 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant polysorbate 80, and 65% w/v polyethylene glycol 300, made up to volume in absolute ethanol. The VPD co-solvent system (VPD:5W) consists of VPD diluted 1:1 with a 5% dextrose in water solution. This co-solvent system dissolves hydrophobic compounds well, and itself produces low toxicity upon systemic administration. Naturally, the proportions of a co-solvent system may be varied considerably without destroying its solubility and toxicity characteristics. Furthermore, the identity of the co-solvent components may be varied: for example, other low-toxicity nonpolar surfactants may be used instead of polysorbate 80; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, e.g. polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose. Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of delivery vehicles or carriers for hydrophobic drugs. Certain organic solvents such as dimethylsulfoxide also may be employed, although usually at the cost of greater toxicity. Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various types of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein or other active ingredient stabilization may be employed.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. Many of the active ingredients of the invention may be provided as salts with pharmaceutically compatible counter ions. Such pharmaceutically acceptable base addition salts are those salts which retain the biological

effectiveness and properties of the free acids and which are obtained by reaction with inorganic or organic bases such as sodium hydroxide, magnesium hydroxide, ammonia, trialkylamine, dialkylamine, monoalkylamine, dibasic amino acids, sodium acetate, potassium benzoate, triethanol amine and the like.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) or other active ingredient(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithins, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent Nos. 4,235,871; 4,501,728; 4,837,028; and 4,737,323, all of which are incorporated herein by reference.

The amount of protein or other active ingredient of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein or other active ingredient of the present invention with which to treat each

individual patient. Initially, the attending physician will administer low doses of protein or other active ingredient of the present invention and observe the patient's response. Larger doses of protein or other active ingredient of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 μg to about 100 mg (preferably about 0.1 μg to about 10 mg, more preferably about 0.1 μg to about 1 mg) of protein or other active ingredient of the present invention per kg body weight. For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein or other active ingredient of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing or other active ingredient-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure

proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxyapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalcium phosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability. Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt %, preferably 1-10 wt % based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells. In further compositions, proteins or other active ingredients of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF-α and TGF-β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins or other active ingredients

of the present invention. The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, *e.g.*, amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (*e.g.*, bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either in vivo or ex vivo into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA). Cells may also be cultured ex vivo in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced in vivo for therapeutic purposes.

4.12.3 EFFECTIVE DOSAGE

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from appropriate in vitro assays. For example, a dose can be formulated in animal models to achieve a circulating

concentration range that can be used to more accurately determine useful doses in humans. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the IC_{50} as determined in cell culture (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of the protein's biological activity). Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD_{50} and ED_{50}. Compounds which exhibit high therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. See, *e.g.*, Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1. Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety which are sufficient to maintain the desired effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from *in vitro* data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen which maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%.

In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

An exemplary dosage regimen for polypeptides or other compositions of the invention will be in the range of about 0.01 μg/kg to 100 mg/kg of body weight daily, with the preferred dose being about 0.1 μg/kg to 25 mg/kg of patient body weight daily, varying in adults and children. Dosing may be once daily, or equivalent doses may be delivered at longer or shorter intervals.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's age and weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

4.12.4 PACKAGING

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may, for example, comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

4.13 ANTIBODIES

Also included in the invention are antibodies to proteins, or fragments of proteins of the invention. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, i.e., molecules that contain an antigen binding site that specifically binds (immunoreacts with) an antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, F_{ab}, $F_{ab'}$ and $F_{(ab')2}$ fragments, and an F_{ab} expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG_1, IgG_2, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain.

Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of the full length protein, such as an amino acid sequence shown in SEQ ID NO: 4, and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region of -related protein that is located on the surface of the protein, *e.g.*, a hydrophilic region. A hydrophobicity analysis of the human related protein sequence will indicate which regions of a related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, *e.g.*, Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, Antibodies: A Laboratory Manual, Harlow E, and Lane D, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

5.13.1 Polyclonal Antibodies

For the production of polyclonal antibodies, various suitable host animals (e.g., rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (e.g., aluminum hydroxide), surface active substances (e.g., lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol; etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and Corynebacterium parvum, or similar immunostimulatory agents. Additional examples of adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (e.g., from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide

primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (The Scientist, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

5.13.2 Monoclonal Antibodies

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or

survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures

such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, Nature 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

5.13.2 Humanized Antibodies

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', $F(ab')_2$ or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536

(1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)).

5.13.3 Human Antibodies

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely

inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (Bio/Technology 10, 779-783 (1992)); Lonberg et al. (Nature 368 856-859 (1994)); Morrison (Nature 368, 812-13 (1994)); Fishwild et al,(Nature Biotechnology 14, 845-51 (1996)); Neuberger (Nature Biotechnology 14, 826 (1996)); and Lonberg and Huszar (Intern. Rev. Immunol. 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the Xenomouse™ as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to

prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

5.13.4 F_{ab} Fragments and Single Chain Antibodies

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see e.g., U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F_{ab} expression libraries (see e.g., Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F_{ab} fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an $F_{(ab')2}$ fragment produced by pepsin digestion of an antibody molecule; (ii) an F_{ab} fragment generated by reducing the disulfide bridges of an $F_{(ab')2}$ fragment; (iii) an F_{ab} fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv) F_v fragments.

5.13.5 Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, Nature, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan).

Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. $F(ab')_2$ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate $F(ab')_2$ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from E. coli and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody $F(ab')_2$ molecule. Each Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody

homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., J. Immunol. 147:60 (1991). Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

5.13.6 Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in

vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

5.13.7 Effector Function Engineering

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design, 3: 219-230 (1989).

5.13.8 Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudomonas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin,

crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi, ^{131}I, ^{131}In, ^{90}Y, and ^{186}Re.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is in turn conjugated to a cytotoxic agent.

4.14 COMPUTER READABLE SEQUENCES

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to

create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and Microsoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data processor structuring formats (*e.g.* text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

By providing any of the nucleotide sequences SEQ ID NO:1-739 or a representative fragment thereof; or a nucleotide sequence at least 95% identical to any of the nucleotide sequences of SEQ ID NO:1-739 in computer readable form, a skilled artisan can routinely access the sequence information for a variety of purposes. Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system is used to identify open reading frames (ORFs) within a nucleic acid sequence. Such ORFs may be protein encoding fragments and may be useful in producing commercially important proteins such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for use in the present invention. As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means. As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of a known sequence which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, Smith-Waterman, MacPattern (EMBL), BLASTN and BLASTA (NPOLYPEPTIDEIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems. As used herein, a "target sequence" can be any nucleic acid or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 300 amino acids, more preferably from about 30 to 100 nucleotide residues. However, it is well recognized that searches for

commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

4.15 TRIPLE HELIX FORMATION

In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA. Polynucleotides suitable for use in these methods are preferably 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 15241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Olmno, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide.

4.16 DIAGNOSTIC ASSAYS AND KITS

The present invention further provides methods to identify the presence or expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using a nucleic acid probe or antibodies of the present invention, optionally conjugated or otherwise associated with a suitable label.

In general, methods for detecting a polynucleotide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polynucleotide of the invention is detected in the sample. Such methods can also comprise contacting a sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of the invention under such conditions, and amplifying annealed polynucleotides, so that if a polynucleotide is amplified, a polynucleotide of the invention is detected in the sample.

In general, methods for detecting a polypeptide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polypeptide of the invention is detected in the sample.

In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the nucleic acid probes of the present invention and assaying for binding of the nucleic acid probes or antibodies to components within the test sample.

Conditions for incubating a nucleic acid probe or antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the nucleic acid probe or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or immunological assay formats can readily be adapted to employ the nucleic acid probes or antibodies of the present invention. Examples of such assays can be found in Chard, T., An Introduction to Radioimmunoassay and Related Techniques, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G.R. et al., Techniques in Immunocytochemistry, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., Practice and Theory of immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985). The test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein

extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention. Specifically, the invention provides a compartment kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the probes or antibodies of the present invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound probe or antibody.

In detail, a compartment kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the antibodies used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which contain the reagents used to detect the bound antibody or probe. Types of detection reagents include labeled nucleic acid probes, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the enzymatic, or antibody binding reagents which are capable of reacting with the labeled antibody. One skilled in the art will readily recognize that the disclosed probes and antibodies of the present invention can be readily incorporated into one of the established kit formats which are well known in the art.

4.17 MEDICAL IMAGING

The novel polypeptides and binding partners of the invention are useful in medical imaging of sites expressing the molecules of the invention (e.g., where the polypeptide of the invention is involved in the immune response, for imaging sites of inflammation or infection). See, e.g., Kunkel et al., U.S. Pat. NO. 5,413,778. Such methods involve chemical attachment of a labeling or imaging agent, administration of

the labeled polypeptide to a subject in a pharmaceutically acceptable carrier, and imaging the labeled polypeptide *in vivo* at the target site.

4.18 SCREENING ASSAYS

Using the isolated proteins and polynucleotides of the invention, the present invention further provides methods of obtaining and identifying agents which bind to a polypeptide encoded by an ORF corresponding to any of the nucleotide sequences set forth in SEQ ID NO:1-739, or bind to a specific domain of the polypeptide encoded by the nucleic acid. In detail, said method comprises the steps of:

(a) contacting an agent with an isolated protein encoded by an ORF of the present invention, or nucleic acid of the invention; and

(b) determining whether the agent binds to said protein or said nucleic acid.

In general, therefore, such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Likewise, in general, therefore, such methods for identifying compounds that bind to a polypeptide of the invention can comprise contacting a compound with a polypeptide of the invention for a time sufficient to form a polypeptide/compound complex, and detecting the complex, so that if a polypeptide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Methods for identifying compounds that bind to a polypeptide of the invention can also comprise contacting a compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a receptor gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, so that if a polypeptide/compound complex is detected, a compound that binds a polypeptide of the invention is identified.

Compounds identified via such methods can include compounds which modulate the activity of a polypeptide of the invention (that is, increase or decrease its activity, relative to activity observed in the absence of the compound). Alternatively, compounds

identified via such methods can include compounds which modulate the expression of a polynucleotide of the invention (that is, increase or decrease expression relative to expression levels observed in the absence of the compound). Compounds, such as compounds identified via the methods of the invention, can be tested using standard assays well known to those of skill in the art for their ability to modulate activity/expression.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention. Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like, capable of binding to a specific peptide sequence, in order to generate rationally designed antipeptide peptides, for example see Hurby et al., Application of Synthetic Peptides: Antisense Peptides," In Synthetic Peptides, A User's Guide, W.H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control. One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix formation by binding to DNA or RNA. Such agents can be based on the classic phosphodiester, ribonucleic acid backbone, or

can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods preferably contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide and other DNA binding agents.

Agents which bind to a protein encoded by one of the ORFs of the present invention can be used as a diagnostic agent. Agents which bind to a protein encoded by one of the ORFs of the present invention can be formulated using known techniques to generate a pharmaceutical composition.

4.19 USE OF NUCLEIC ACIDS AS PROBES

Another aspect of the subject invention is to provide for polypeptide-specific nucleic acid hybridization probes capable of hybridizing with naturally occurring nucleotide sequences. The hybridization probes of the subject invention may be derived from any of the nucleotide sequences SEQ ID NO:1-739. Because the corresponding gene is only expressed in a limited number of tissues, a hybridization probe derived from of any of the nucleotide sequences SEQ ID NO:1-739 can be used as an indicator of the presence of RNA of cell type of such a tissue in a sample.

Any suitable hybridization technique can be employed, such as, for example, in situ hybridization. PCR as described in US Patents Nos. 4,683,195 and 4,965,188 provides additional uses for oligonucleotides based upon the nucleotide sequences. Such probes used in PCR may be of recombinant origin, may be chemically synthesized, or a mixture of both. The probe will comprise a discrete nucleotide sequence for the detection

of identical sequences or a degenerate pool of possible sequences for identification of closely related genomic sequences.

Other means for producing specific hybridization probes for nucleic acids include the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art and are commercially available and may be used to synthesize RNA probes *in vitro* by means of the addition of the appropriate RNA polymerase as T7 or SP6 RNA polymerase and the appropriate radioactively labeled nucleotides. The nucleotide sequences may be used to construct hybridization probes for mapping their respective genomic sequences. The nucleotide sequence provided herein may be mapped to a chromosome or specific regions of a chromosome using well known genetic and/or chromosomal mapping techniques. These techniques include in situ hybridization, linkage analysis against known chromosomal markers, hybridization screening with libraries or flow-sorted chromosomal preparations specific to known chromosomes, and the like. The technique of fluorescent in situ hybridization of chromosome spreads has been described, among other places, in Verma et al (1988) Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York NY.

Fluorescent *in situ* hybridization of chromosomal preparations and other physical chromosome mapping techniques may be correlated with additional genetic map data. Examples of genetic map data can be found in the 1994 Genome Issue of Science (265:1981f). Correlation between the location of a nucleic acid on a physical chromosomal map and a specific disease (or predisposition to a specific disease) may help delimit the region of DNA associated with that genetic disease. The nucleotide sequences of the subject invention may be used to detect differences in gene sequences between normal, carrier or affected individuals.

4.20 PREPARATION OF SUPPORT BOUND OLIGONUCLEOTIDES

Oligonucleotides, i.e., small nucleic acid segments, may be readily prepared by, for example, directly synthesizing the oligonucleotide by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer.

Support bound oligonucleotides may be prepared by any of the methods known to those of skill in the art using any suitable support such as glass, polystyrene or Teflon. One strategy is to precisely spot oligonucleotides synthesized by standard synthesizers.

Immobilization can be achieved using passive adsorption (Inouye & Hondo, (1990) J. Clin. Microbiol. 28(6) 1469-72); using UV light (Nagata *et al.*, 1985; Dahlen *et al.*, 1987; Morrissey & Collins, (1989) Mol. Cell Probes 3(2) 189-207) or by covalent binding of base modified DNA (Keller *et al.*, 1988; 1989); all references being specifically incorporated herein.

Another strategy that may be employed is the use of the strong biotin-streptavidin interaction as a linker. For example, Broude *et al.* (1994) Proc. Natl. Acad. Sci. USA 91(8) 3072-6, describe the use of biotinylated probes, although these are duplex probes, that are immobilized on streptavidin-coated magnetic beads. Streptavidin-coated beads may be purchased from Dynal, Oslo. Of course, this same linking chemistry is applicable to coating any surface with streptavidin. Biotinylated probes may be purchased from various sources, such as, e.g., Operon Technologies (Alameda, CA).

Nunc Laboratories (Naperville, IL) is also selling suitable material that could be used. Nunc Laboratories have developed a method by which DNA can be covalently bound to the microwell surface termed Covalink NH. CovaLink NH is a polystyrene surface grafted with secondary amino groups (>NH) that serve as bridge-heads for further covalent coupling. CovaLink Modules may be purchased from Nunc Laboratories. DNA molecules may be bound to CovaLink exclusively at the 5'-end by a phosphoramidate bond, allowing immobilization of more than 1 pmol of DNA (Rasmussen *et al.*, (1991) Anal. Biochem. 198(1) 138-42).

The use of CovaLink NH strips for covalent binding of DNA molecules at the 5'-end has been described (Rasmussen et al., (1991). In this technology, a phosphoramidate bond is employed (Chu et al., (1983) Nucleic Acids Res. 11(8) 6513-29). This is beneficial as immobilization using only a single covalent bond is preferred. The phosphoramidate bond joins the DNA to the CovaLink NH secondary amino groups that are positioned at the end of spacer arms covalently grafted onto the polystyrene surface through a 2 nm long spacer arm. To link an oligonucleotide to CovaLink NH via an phosphoramidate bond, the oligonucleotide terminus must have a 5'-end phosphate group. It is, perhaps, even possible for biotin to be covalently bound to CovaLink and then streptavidin used to bind the probes.

More specifically, the linkage method includes dissolving DNA in water (7.5 ng/ul) and denaturing for 10 min. at 95°C and cooling on ice for 10 min. Ice-cold 0.1 M

1-methylimidazole, pH 7.0 (1-MeIm$_7$), is then added to a final concentration of 10 mM 1-MeIm$_7$. A ss DNA solution is then dispensed into CovaLink NH strips (75 ul/well) standing on ice.

Carbodiimide 0.2 M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC), dissolved in 10 mM 1-MeIm$_7$, is made fresh and 25 ul added per well. The strips are incubated for 5 hours at 50°C. After incubation the strips are washed using, e.g., Nunc-Immuno Wash; first the wells are washed 3 times, then they are soaked with washing solution for 5 min., and finally they are washed 3 times (where in the washing solution is 0.4 N NaOH, 0.25% SDS heated to 50°C).

It is contemplated that a further suitable method for use with the present invention is that described in PCT Patent Application WO 90/03382 (Southern & Maskos), incorporated herein by reference. This method of preparing an oligonucleotide bound to a support involves attaching a nucleoside 3'-reagent through the phosphate group by a covalent phosphodiester link to aliphatic hydroxyl groups carried by the support. The oligonucleotide is then synthesized on the supported nucleoside and protecting groups removed from the synthetic oligonucleotide chain under standard conditions that do not cleave the oligonucleotide from the support. Suitable reagents include nucleoside phosphoramidite and nucleoside hydrogen phosphorate.

An on-chip strategy for the preparation of DNA probe for the preparation of DNA probe arrays may be employed. For example, addressable laser-activated photodeprotection may be employed in the chemical synthesis of oligonucleotides directly on a glass surface, as described by Fodor *et al.* (1991) Science 251(4995) 767-73, incorporated herein by reference. Probes may also be immobilized on nylon supports as described by Van Ness *et al.* (1991) Nucleic Acids Res. 19(12) 3345-50; or linked to Teflon using the method of Duncan & Cavalier (1988) Anal. Biochem. 169(1) 104-8; all references being specifically incorporated herein.

To link an oligonucleotide to a nylon support, as described by Van Ness *et al.* (1991), requires activation of the nylon surface via alkylation and selective activation of the 5'-amine of oligonucleotides with cyanuric chloride.

One particular way to prepare support bound oligonucleotides is to utilize the light-generated synthesis described by Pease *et al.*, (1994) PNAS USA 91(11) 5022-6,

incorporated herein by reference). These authors used current photolithographic techniques to generate arrays of immobilized oligonucleotide probes (DNA chips). These methods, in which light is used to direct the synthesis of oligonucleotide probes in high-density, miniaturized arrays, utilize photolabile 5'-protected *N*-acyl-deoxynucleoside phosphoramidites, surface linker chemistry and versatile combinatorial synthesis strategies. A matrix of 256 spatially defined oligonucleotide probes may be generated in this manner.

4.21 PREPARATION OF NUCLEIC ACID FRAGMENTS

The nucleic acids may be obtained from any appropriate source, such as cDNAs, genomic DNA, chromosomal DNA, microdissected chromosome bands, cosmid or YAC inserts, and RNA, including mRNA without any amplification steps. For example, Sambrook *et al.* (1989) describes three protocols for the isolation of high molecular weight DNA from mammalian cells (p. 9.14-9.23).

DNA fragments may be prepared as clones in M13, plasmid or lambda vectors and/or prepared directly from genomic DNA or cDNA by PCR or other amplification methods. Samples may be prepared or dispensed in multiwell plates. About 100-1000 ng of DNA samples may be prepared in 2-500 ml of final volume.

The nucleic acids would then be fragmented by any of the methods known to those of skill in the art including, for example, using restriction enzymes as described at 9.24-9.28 of Sambrook *et al.* (1989), shearing by ultrasound and NaOH treatment.

Low pressure shearing is also appropriate, as described by Schriefer *et al.* (1990) Nucleic Acids Res. 18(24) 7455-6, incorporated herein by reference). In this method, DNA samples are passed through a small French pressure cell at a variety of low to intermediate pressures. A lever device allows controlled application of low to intermediate pressures to the cell. The results of these studies indicate that low-pressure shearing is a useful alternative to sonic and enzymatic DNA fragmentation methods.

One particularly suitable way for fragmenting DNA is contemplated to be that using the two base recognition endonuclease, *Cvi*JI, described by Fitzgerald *et al.* (1992) Nucleic Acids Res. 20(14) 3753-62. These authors described an approach for the rapid fragmentation and fractionation of DNA into particular sizes that they contemplated to be suitable for shotgun cloning and sequencing.

The restriction endonuclease *CviJI* normally cleaves the recognition sequence PuGCPy between the G and C to leave blunt ends. Atypical reaction conditions, which alter the specificity of this enzyme (*CviJI***), yield a quasi-random distribution of DNA fragments form the small molecule pUC19 (2688 base pairs). Fitzgerald *et al.* (1992) quantitatively evaluated the randomness of this fragmentation strategy, using a *CviJI*** digest of pUC19 that was size fractionated by a rapid gel filtration method and directly ligated, without end repair, to a lac Z minus M13 cloning vector. Sequence analysis of 76 clones showed that *CviJI*** restricts pyGCPy and PuGCPu, in addition to PuGCPy sites, and that new sequence data is accumulated at a rate consistent with random fragmentation.

As reported in the literature, advantages of this approach compared to sonication and agarose gel fractionation include: smaller amounts of DNA are required (0.2-0.5 ug instead of 2-5 ug); and fewer steps are involved (no preligation, end repair, chemical extraction, or agarose gel electrophoresis and elution are needed

Irrespective of the manner in which the nucleic acid fragments are obtained or prepared, it is important to denature the DNA to give single stranded pieces available for hybridization. This is achieved by incubating the DNA solution for 2-5 minutes at 80-90°C. The solution is then cooled quickly to 2°C to prevent renaturation of the DNA fragments before they are contacted with the chip. Phosphate groups must also be removed from genomic DNA by methods known in the art.

4.22 PREPARATION OF DNA ARRAYS

Arrays may be prepared by spotting DNA samples on a support such as a nylon membrane. Spotting may be performed by using arrays of metal pins (the positions of which correspond to an array of wells in a microtiter plate) to repeated by transfer of about 20 nl of a DNA solution to a nylon membrane. By offset printing, a density of dots higher than the density of the wells is achieved. One to 25 dots may be accommodated in 1 mm^2, depending on the type of label used. By avoiding spotting in some preselected number of rows and columns, separate subsets (subarrays) may be formed. Samples in one subarray may be the same genomic segment of DNA (or the same gene) from different individuals, or may be different, overlapped genomic clones. Each of the subarrays may represent replica spotting of the same samples. In one example, a selected gene segment may be amplified from 64 patients. For each patient, the amplified gene segment may be in one 96-well plate

(all 96 wells containing the same sample). A plate for each of the 64 patients is prepared. By using a 96-pin device, all samples may be spotted on one 8 x 12 cm membrane. Subarrays may contain 64 samples, one from each patient. Where the 96 subarrays are identical, the dot span may be 1 mm^2 and there may be a 1 mm space between subarrays.

Another approach is to use membranes or plates (available from NUNC, Naperville, Illinois) which may be partitioned by physical spacers e.g. a plastic grid molded over the membrane, the grid being similar to the sort of membrane applied to the bottom of multiwell plates, or hydrophobic strips. A fixed physical spacer is not preferred for imaging by exposure to flat phosphor-storage screens or x-ray films.

The present invention is illustrated in the following examples. Upon consideration of the present disclosure, one of skill in the art will appreciate that many other embodiments and variations may be made in the scope of the present invention. Accordingly, it is intended that the broader aspects of the present invention not be limited to the disclosure of the following examples. The present invention is not to be limited in scope by the exemplified embodiments which are intended as illustrations of single aspects of the invention, and compositions and methods which are functionally equivalent are within the scope of the invention. Indeed, numerous modifications and variations in the practice of the invention are expected to occur to those skilled in the art upon consideration of the present preferred embodiments. Consequently, the only limitations which should be placed upon the scope of the invention are those which appear in the appended claims.

All references cited within the body of the instant specification are hereby incorporated by reference in their entirety.

5.0 EXAMPLES

5.1 EXAMPLE 1

Novel Nucleic Acid Sequences Obtained From Various Libraries

A plurality of novel nucleic acids were obtained from cDNA libraries prepared from various human tissues and in some cases isolated from a genomic library derived from human chromosome using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The inserts of the library were amplified with PCR using primers specific for the vector sequences which flank the inserts. Clones from cDNA libraries were

spotted on nylon membrane filters and screened with oligonucleotide probes (e.g., 7-mers) to obtain signature sequences. The clones were clustered into groups of similar or identical sequences. Representative clones were selected for sequencing.

In some cases, the 5' sequence of the amplified inserts was then deduced using a typical Sanger sequencing protocol. PCR products were purified and subjected to fluorescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer to obtain the novel nucleic acid sequences. In some cases RACE (Random Amplification of cDNA Ends) was performed to further extend the sequence in the 5' direction.

5.2 EXAMPLE 2

Novel Contigs

The novel contigs of the invention were assembled from sequences that were obtained from a cDNA library by methods described in Example 1 above, and in some cases sequences obtained from one or more public databases. Chromatograms were base called and assembled using a software suite from University of Washington, Seattle containing three applications designated PHRED, PHRAP, and CONSED. The sequences for the resulting nucleic acid contigs are designated as SEQ ID NO: 1-739 and are provided in the attached Sequence Listing. The contigs were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend the seed EST into an extended assemblage, by pulling additional sequences from different databases (i.e., Hyseq's database containing EST sequences, dbEST version 120, gb pri 120, UniGene version 120, and Genpept 120) that belong to this assemblage. The algorithm terminated when there was no additional sequences from the above databases that would extend the assemblage. Inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

The nearest neighbor result for the assembled contig was obtained by a FASTA version 3 search against Genpept release 120, using FASTXY algorithm. FASTXY is an improved version of FASTA alignment which allows in-codon frame shifts. The nearest neighbor result showed the closest homologue for each assemblage from Genpept (and

contains the translated amino acid sequences for which the assemblage encodes). The nearest neighbor results for SEQ ID NO: 1-739 are shown in Table 2.

Tables 1, 2, and 3 follow. Table 1 shows the various tissue sources of SEQ ID NO: 1-739. Table 2 shows the nearest neighbor result for the assembled contig. The nearest neighbor result shows the closest homologue for each assemblage and contains the translated amino acid sequences for which the assemblage encodes. Table 2 also shows homologues with identifiable functions for SEQ ID NO: 1-739. The polypeptides were predicted using a software program called FASTY (available from http://fasta.bioch.virginia.edu) which selects a polypeptide based on a comparison of translated novel polynucleotides to known polynucleotides (W.R. Pearson, Methods in Enzymology, Vol. 183: pp. 63-98, (1990), herein incorporated by reference). Table 3 shows the predicted amino acid sequence corresponding to the novel nucleic acid contig sequences.

Table 1 - Tissue Sources

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
adult brain	GIBCO	AB3001	28 46 54 62 95 117 134 175 188-189 324 330 337 356 369 371 378 386 389 396 432 435-436 468 472-473 476-477 483 486 518 538-539 543 545 557 565 571 573 578 582 598 613-614 619 627 632 634 639 687 709
adult brain	GIBCO	ABD003	5 12 46 52 57 66 79 91 97 134 144 148 150 162 164 172 175-176 181 186 193 250 323 325-327 330 334 338 362 367 369 371 378-379 386 388-389 392 396-397 399-401 403 416 422 435 444 449 451 454 461 463-464 468 472-473 483 486 494 506 511 513 516 520 523-524 526 529 533 536-537 539 545 548 552 556 558-559 562-563 565 567 569 573-574 576 579-580 582-584 590 593-594 598 602 606 613-614 619-621 623-624 627 634 637 641 646 648 659 675 688-689 694 696-698 703 714 729
adult brain	Clontech	ABR001	57 162 164 227 266 316 334 356 367 385 438 468 512 524 528 557 582 590 621 627 631 634 689 714
adult brain	Clontech	ABR006	189 228 385 438 571 584 632 650 677
adult brain	Clontech	ABR008	1 3 5 11-25 31-32 46-47 55-57 59

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			61 65-67 69 75 79 91 103 108 111 113-114 126 132 150 160 162 164 171-172 186 188-189 193 202-203 206 210-212 220 222-224 227-229 233 235-236 243-247 251-252 257 264-266 268 275 313 324 328-331 334-335 338-339 343 346-347 351 355 357 359-361 365 367 370-371 378 380 382 386-389 391 396 399-400 402 406 413 419-420 423 426 432 434 437-438 442 446 448-449 459-460 465 468 470 472-473 475 481-483 487 489-490 495-497 499 501 503-504 507-509 511 520 524 526 528 532-533 536 539-540 543-546 551-552 556-557 563 565-567 569 572-573 576-577 579-580 582 584 586 590-591 593 595-597 599-602 604 610-616 620-621 624-625 627-628 632 634 637-638 641 643-644 646-647 650 653-657 660-662 668 672 675 677-678 680-681 688-689 691 693 695-696 698 706-707 709 711 713-727 729 731 733-734 736 738-739
adult brain	Clontech	ABR011	334 476 634 677
adult brain	BioChain	ABR012	379 587
adult brain	Invitrogen	ABR013	334 634
adult brain	Invitrogen	ABT004	3 19 57 62 66 75 110 122 150 160 162 167 171 176 186 197 203 211 230 232 259 328-331 334 369 382 389 394 400 406 417 426 429 442 457 472 483-484 492 511 514 529 531 534 537 540 553 558 562 572 580 582-584 590 604 611 613 615 622 637 639 643-644 648 688-689 692 695
cultured preadipo-cytes	Strategene	ADP001	16 37-39 66 109 120 141 144 193 273 316 331 333 338 389 415 429 442 444 464-465 475 489 501 511 513 531 534 539-540 545-546 557 583-584 590 596 602 607 613 615 619 622 629 632 634 643
adrenal gland	Clontech	ADR002	4-5 12 48 53 57 162 164 172 186 188 192 196 203 207 213 258 316 330-331 333 339 354 356-357 369 383 385 388 392 395 402 406 411 415 434 454-455 465 468 473 475 477 491 498 501 509 511 517 528-529 532 537-539 542 545 558 560 565 567 576-577 586 600 606 615 621 624 627 632 634 647 653 660 667 683 689 696 714

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
adult heart	GIBCO	AHR001	28 39 57 64-65 75 79 89 97-98 108 117 134 144 157 159-160 164-166 169 171 174 184 192-193 203 207 220 243 256 258 266-267 281 314 316 318 328-329 331 338-339 341 346 348 354 356-357 366-367 369 371 377-379 382 385-386 388 393 395-396 399-401 403 415 420 422 425 431-432 435-436 445 451 459 465 472-473 477 483 486 488 490 496 501 503 508 515 519-520 526 528 531 533-534 537-538 540-541 544 546 552 556-557 562-563 566-571 573 576-581 583-584 586-587 594 602 606 608 611 613-615 618 620-621 626-628 632 634 641 643 646 648 653 659 667 676 678 687 689 696 703-704 708 711 714 729-730
adult kidney	GIBCO	AKD001	3 28-29 48 56-57 67 79 84 93 106 117 134 138 140 144 156 160-164 168-170 172 177 183 188-189 192-193 199 203 207 235 251 257 275 319 321-323 328-330 337 346-347 349 354-356 360 367-369 371 375 378-381 383-386 388-389 392 396-397 399 401 404 407 409 411-412 415-416 420-422 427 432 436-437 439-440 444 451-456 458-459 464-465 468 470 472-473 477 481 483 486-487 492 496 501 503 505-506 508 511 513-516 518 524 526 529 533 535 537-541 543 545-546 548 552 557 559-560 562-563 565-569 572-574 576-577 579-587 589-591 593-594 602 604-607 613-614 617-618 620-624 627-628 630 632-635 637-638 640-642 644-645 652 662 664 667-668 677 682 685 687 689 694-696 698 703 716 723 728-729 732 734
adult kidney	Invitrogen	AKT002	92 136 154 160 164 178 271 314 347 353 360 367 376 378-379 386 391 402 409 423 432 449 451 477 490 494 503 526 528 531 534 538-539 541 545-546 559 566 579 584 588 594 602 613 621 624 632 647 652 689
adult lung	GIBCO	ALG001	56-57 67 69 98 113 134 144 164 172 191-192 270 321 328 338 369 371 374 378 380 388-389 396 405 411 416 424 443-444 456 473-474 482-483 497 508 518 529 531 534 536

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			540 552 556 559 563 568 573 579-580 585-586 588-589 593 601-602 606 612-613 618 634 662 667 685 696 702 726 729-730
lymph node	Clontech	ALN001	28 57 79 113 164 172 179 193 240 325 332 367 378-379 386 388 402 485 526 580 586 603 613-614 621-622 628 634 662 667 686 734
young liver	GIBCO	ALV001	3 24 28 54 60 117 134 137 154 160 193 196 242 273 316 328-329 334 351 354 370-371 388 392 395-396 401 406 411 415 432 435 439 448 454-455 477 483 486-487 495 506 509 514 518 523-524 526 529 531 534 537-538 540 544 548 566 568 571 573 579 587-588 591 594 602 621 641 645 686 713 723
adult liver	Invitrogen	ALV002	3 24 27 56-57 65-66 71 79 92 97 106 134 140 164 192 200 214 220 232 240 242 271-272 291 313 316 328 347 349-350 353 355 357 368-369 371-372 378-379 381-382 385 397 430 435 448 457 459 471-472 475 485 487 502 505-506 511 520 530-531 533-534 537 540-541 543 548 566 574-575 579 582 588 590 612 623 640 648-649 681 687 689 710 714
adult ovary	Invitrogen	AOV001	3 10 14 28 54 56-58 62 65-66 68 73 75 79 98 127 144 154 162 164-165 172-174 182 186 188-189 192-196 206 213 224 234-235 241 243 248 253 261 273 275 289 314 316 321-322 325-327 329-331 333-334 336-338 340 343 345-348 354-357 367 369 371-372 378 382 386 388 395-397 399-402 404 407 411 415-416 419-420 425 427 429 431 435-437 441 444 451 453-459 465 468-470 472-475 481 485 490 494 496 501 503 509-510 513 517-518 522-524 526 528-529 531-534 537-542 545-546 548 552 554 556-557 559-560 562-563 565 567-569 572-579 581-582 584-588 590-591 593-598 602-604 606 611-615 618 620-623 627 629 631-632 635-638 643 647 652-654 657 659 661-662 667 674-675 677-678 682 684 689 693 695-698 703 705-707 714 717-718 723 729 731 738
adult placenta	Clontech	APL001	172 224 239 363 371 392 437 531 534 622 690 696

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
placenta	Invitrogen	APL002	57 66 122 161 172 241 326 329 334 369 388 407 427 429 436 459 464 506 508 511 539 541 545 566 573 575 590 597 637 648 690
adult spleen	GIBCO	ASP001	28 57 65 78 93 95 117 134 156-157 172 186 188 194 214 273 314 319 331 334 338 344 354 371 374 392 436 457 471-473 478-479 481 483 515 526 528-529 541 548 557 559 563 565 569 573 585-587 603 606 613 615 618 621-622 627 632 634 637 643 654 671 689 696-698 701 712 739
testis	GIBCO	ATS001	3 67 134 160 192 235 327 329 337 342 371 375 378 380-381 396 399 415 431 436 441 451 472 477-478 483 486 494 496 503 522 524 526 531 533-534 538 541-542 546 548 557 568 573 577 579 581 584 594 596 618 641 658 662 689 700 714 729-730
adult bladder	Invitrogen	BLD001	28 57 112 161 164 172 192 194 250 334 354 370 397 404 487 513 526 531 534 545 572 599 602 620 634 651 659 672 689 713 725
bone marrow	Clontech	BMD001	10-11 28 31 54 57 62 75 78-83 88 131-133 135-137 141-143 157 159 164 171-173 176-177 187-189 192 195 200 202 205 207 218 225 282 314-318 325 330 334-335 337 346-348 367 369 372 378 383 386 388 395 401 405 412-413 416 422 436 442-443 447 449 455 465 472 475 477 503 516 523 528-529 533-534 539 545 551 556 559 563 565-567 571 573-574 576 579-586 594 601-602 606 613 620-623 628-629 634 638 642-643 646 656 659 666 686 689 691 696 698-699 703 705 714 720 726 729
bone marrow	Clontech	BMD002	2 15 23 35 49 54 57 59 78 81 114 156-157 164 171-172 189-190 202 223 240 325 334 346 357 367 379 381-382 388 397 412 454 465 482 490 509 516 526 535 537 563 566 579 595 600 638 640-641 654-655 676 689 714
adult colon	Invitrogen	CLN001	48 79 94 138 162 167 189 333 368-369 375 386 404 409 414 435-436 455 470 525 541 548 553 567 603 634 656 659 689 694 721
adult cervix	BioChain	CVX001	3 28 35 54 57 79 83 95 97 113 117 154 162 164 172 176 220 235 248-

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			249 321 327 329 333 338 346 348 354 356 362 367-368 371 374-375 378-379 386 388-389 395 401-402 404 407 420 429 431 437 443 451 459 468 475 477 479 483 485 490 493-494 496 506 508 511 517 526 528 531 534 544 550 552 559 566 569 571-573 575-576 581-583 588 590 593-594 604 606 614 622 628 631-635 639 661-662 675 689 692 695 715 718 738
endothelial cells	Strategene	EDT001	3 28 31 39 54 58 65-66 79 89 144 160 173 187 189 191 193 197-199 207 220 230 267 273 314 324 326 329-331 336 347 354 369 372 378-379 384 386 388 391-394 396-397 399 401 407 420 422 429 431-432 435-437 444 449 451 455 459 465 472 474-475 481-482 486 490 499-501 503 506 511 513 515-517 520 522-524 528 531-534 538-539 541 545-546 548 550 552 557 559-560 563 565 567 569 571 573 577 579-580 583-584 587-590 593-594 596-597 599 602 611 614-615 618 620-621 624 630 632-634 637-638 642-643 647-648 651 675 677 680 682 694 696-698 703 708 714 719 724-725 728-730 734
Genomic clones from the short arm of chromosome 8	Genomic DNA from Genetic Research	EPM001	38 41-45 118-121 164 198 292-312
Genomic clones from the short arm of chromosome 8	Genomic DNA from Genetic Research	EPM003	43 164 295
Genomic clones from the short arm of chromosome 8	Genomic DNA from Genetic Research	EPM004	121 164 306 482
Genomic clones from the short arm of chromosome 8	Genomic DNA from Genetic Research	EPM006	293

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
esophagus	BioChain	ESO002	513 526
fetal brain	Clontech	FBR001	57 468 563 634
fetal brain	Clontech	FBR004	162 186 254 265 491 582
fetal brain	Clontech	FBR006	1-2 5-6 11-12 22-23 49 57 62 73 94 103 114 162 164 172 189 193 203 218 240 244 251-252 259 279 330-331 334-335 346-347 351 367 378 386 388-389 399 413 420 422 424 434 442 444 448 465 468 470 472-473 490 496 501 503-504 511 520 524 528 532-533 539 544-546 548 551 553 563 571 573 576 587 591 601 613 615-616 620-621 628 634 641 644 648 653 657 662 672-673 689 691 698 706 714 718 725-728 733 735-739
fetal brain	Clontech	FBRs03	444 587
fetal brain	Invitrogen	FBT002	17 66 157 162 164 186 190 193 250 270 324 331 334-335 338 346 354-355 374 382 389-390 426 429-430 437 442 453 467 471 475 481 485 491 507-508 513-514 526 528 532 540 544 548 550 552-553 557-558 563 565-566 590 593 602 612 615 637 641 648 654 662 672 676 692 703
fetal heart	Invitrogen	FHR001	57 75 164 547
fetal kidney	Clontech	FKD001	57 164 172 179 188 194 208 218 230 240 250 330 334 369 388 401 413 439 454 465 529 546 550 573 576 581 583 594-596 602 634 648 667 676 689 698 706
fetal kidney	Clontech	FKD002	2 560
fetal kidney	Invitrogen	FKD007	565 596-597
fetal lung	Clontech	FLG001	75 164 355 386 428 455 513 524 528 631 689
fetal lung	Invitrogen	FLG003	30 157 162 169 188 243 253 256 283 330 392 400-401 404 407 424 428 435-436 479 506 508 520 530-531 534 572 578 584 602 611 613 631 654 658 662 676 689 701 716
fetal lung	Clontech	FLG004	371
fetal liver-spleen	Columbia University	FLS001	2-3 5 26 29 31 35 48 54-58 60 62 65 67 70 74-77 79-80 84-87 89 92 96 98-100 104 117 122-130 138 140 144-158 160 162 164 172-173 185-186 188-189 192-194 196 199-200 207 214 218-219 237-238 241 269 273 280 282 314-316 318-322 324 327 329-331 334-335 337 340 345 348-350 354-358 363-364 367-371

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			373 375 377-380 382-383 385-386 388 394-396 399 402 409 411-412 418 420-422 424 427 431 435-437 440 442 448-451 453 455 459 461 464-465 470 472-473 475 477-478 480-485 488-490 501 503 505-506 509 511-513 515-518 520 522-524 526-534 538-539 541 543-547 549-550 552-553 556-557 559-564 566-567 569 571 573 576 578-580 582-587 589 591-594 596-597 599-600 602 611-615 618 620-625 627-628 631-636 638 641-642 646 648 651 659-660 662-664 667-668 675-678 680-681 684 689-690 696-698 709 714 723 738
fetal liver-spleen	Columbia University	FLS002	15 31-32 39-40 47-49 52 56 60 65 69 72 75 78 84 97-98 100 104 115 123 138 140 144 146 152-153 157 161 164 172-173 182 188 194 196 199 220 241-242 246 249 253 255 266 273-275 280-281 288-291 314-316 318-319 321-322 324 329-331 336-339 343 347-350 353-354 357-358 363 367 369-370 372 374 378-380 382-383 386 388-389 393-397 399 405 407 409-410 412 421 424 432 435 439 448 450-451 453-457 459 461 464-465 470 472-475 477 479-481 483 485 488 490 497 501 503 506 509 511-513 516-518 520 524 527-528 531-532 534 539 541-546 556 559-560 565-566 569 571 574 576 579 582-586 588 590 597-599 602-604 606 615 618 620-621 623 625 627 632-634 639 641 644 648 666-668 675-676 681 684 689-690 696-697 701 703 714 719 723 734-735
fetal liver-spleen	Columbia University	FLS003	60 79 157 190 690
fetal liver	Invitrogen	FLV001	3 27 35 48 50 56-57 66 75 92 94 105 157 161 164 176 189 209 220 243 272 324 328 333 335 353 369-370 381 392 396 429-430 435 439-440 442 444 465 471 483 487 502 506 513-514 519 534-535 537 548 554 566 568 576-577 580 582 590 613 621 645 648-649 689
fetal liver	Clontech	FLV002	343
fetal muscle	Invitrogen	FMS001	51 79 97 108-110 166 194 196 266 341 352 380 389 402 407 444 464

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			475 501 513 524 546 552 554 560 570 572 598 605 628 634 649 675 703-704 714 737
fetal muscle	Invitrogen	FMS002	524
fetal skin	Invitrogen	FSK001	31 33 35 48 57 63 67 75 112-114 117 157 162 164 172 178 180 188 196 220 243 254 319 324 328 330 333-334 367 369 371 375 379-383 386 388-389 400 404 407 412 419-420 429 444 455 472-473 491 499 503 508 511 514 517 522-524 529 531 534 537 540 542 547 552 554 556-557 560 563 565 567 571-572 574 576 579 590 596 599 616 621 625 627 631-632 634 639-640 648 653-654 662 689 708 714
fetal skin	Invitrogen	FSK002	501 537
fetal spleen	BioChain	FSP001	465 729
umbilical cord	BioChain	FUC001	27-28 35 57 68 83 105 136 157 159-160 164 188 191 225 279 315-316 321 328 334 363 367 369 378-379 383 386 388-389 392 397 406-407 413 415-416 427 440 449 455 458 461 464-465 468 473-475 479 485-486 488 490 496 514 517 522 524 526 528-529 531 533-534 538 540 546 550 552 556-558 572 582 584-585 587-588 594-597 602 606 613 616 618-619 631 634 637 651 689 696 698 706 729
fetal brain	GIBCO	HFB001	3 5 22 26 46 53 66 73 94 117 134 139 164 172-173 188-189 212 215 230-231 248 251 262 288-289 316 325 329-331 334 337-338 348 352 365-367 369 371 377-379 385-386 388 392 394 396 400 403 420 422 429 437 444-446 449 451 455 459 461-463 466-468 472-473 475 477 481 483 485-486 488 490-491 496 503-504 506 513 523-524 529 532-533 539-541 545 548 550 552 557-560 563 565-566 569 571 576-577 579-580 583-584 586 590 593-594 596-599 601-602 604 606 611 613 615 618 621-623 627-628 634-635 637 641 643 647 662 664-665 667 675 677 680 689 695-697 703 726
macrophage	Invitrogen	HMP001	97 518 532 569
infant brain	Columbia University	IB2002	28 46 56-57 59 67 75 78 109 117 122 129 144 157 162 164-165 172 176 180 190 193 212 220 226 236-

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			237 251 261-262 316 318 324 328-330 334-335 337 340 354-356 361 364-365 367 369 371-373 377-380 382 385-386 389 392 395 397 400 411 416 421-422 429 432 436 438 444 448 451 456 464-465 469 471-475 484 486 496 504-506 511 520 524 526 529 531 533-534 537-540 544-546 548 553 556 558 562 565 567 576 579-580 582 584 586 589-590 593 597-598 602 613-614 618 620-621 627-628 632 634 636 641 650 654 659 662 667 683 689 721 730
infant brain	Columbia University	IB2003	46 54 75 109 156 164 220 244 251 314 324-325 331 335 340 361-362 367 369 377-379 400 408 438 442 456 460 464 469 472 496 506 523-524 526 529 538 540 544-545 547 558 560-562 565 567 569 579 584 598 602 613 615 621 627 632 634 637 639 650 738
infant brain	Columbia University	IBM002	262 340 432 436 438 472 531 534 569 613 634
infant brain	Columbia University	IBS001	162 231 283 331 369 385 438 444 472 506 513 523 531 534 580 615 636 689
lung, fibroblast	Strategene	LFB001	28 54 57 65 172 188 233 321 331 340 347 367 369 378-379 388 401 451 459 475 479 503 511 522 524 532 534 559-560 573 580 583 587 597 615 632 634 638 686 689 708
lung tumor	Invitrogen	LGT002	3 7 21 24 26 28 31 54 56-57 62-63 66 92-93 101 109 112 162 164 171-172 176 183 188-189 192-193 196 201-202 223 230 235 259 273-274 316 321 329-331 333-334 338 345 347-348 356 367 369 371-372 378-379 381-382 386 388-390 396 399-404 406 409 416 424-425 427 429 432 436-437 439 451 455-456 459 464-465 467 473 475 484-486 490 499 502-503 506 508 511 513-514 517-518 522 524 526 528 531-532 534-535 538-539 541 543-546 553 557-559 563 567-568 571 573 575-576 579-580 585-588 590-591 593-594 598 601-604 609 611-613 615 621 627-628 631-632 636-637 645 648 651-652 654 662 667 672 677 681 683 689 698 701-702 714 718 724 726 729 734
lymphocytes	ATCC	LPC001	4 31-32 35 57 65-66 70 110 116 156

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			162 164 230 243 250 282 287 326 328-330 334 336 346-347 359 378 386 388 397 407 414 416 419 472 497 520 525 539 545 549 551 582 590 606 615 618 621 631 634 686 692 698 701 714
leukocyte	GIBCO	LUC001	4 7 9-11 23 28 31 35 39 54 65 75-76 79 90 97 110 117 134 152 157 159 162 164-167 171 173 176 188 193 199 204 207 220 244 253 255 314 316 318 321 324 326 329-330 337-339 346-347 352 354 356 367 369 371 378-379 382 388-389 392 396-397 400-402 405 415-416 420 422 429 432 435-436 443-444 449 454-455 457-459 465 479 481-486 491 497 501 503-504 506 508 511 514 516 520 523-525 529 532-533 535 538-539 545 548 552-554 556 559-560 562-563 565-566 569 571-573 576 579 581 585-587 590 593-594 598 600-602 604 606-609 613-614 618 620-622 624 627 630 632-634 636 638 643 645 660-662 667 678 682 684 686 689 691 693 696-698 714 726
leukocyte	Clontech	LUC003	11 54 97 152 164 330 479 546 564-565 593 613 627 634 646 696 729
melanoma from cell line ATCC #CRL 1424	Clontech	MEL004	2 57 67 79 164 171-173 188 193 196 232 321 337 341 346 367 379-380 388 407 427 454 472 477 482 501 520 539 545 552 556 579 588 593 598 611 621 631 648 665 714 730
mammary gland	Invitrogen	MMG001	3 20-21 29 31 54 56-57 63-66 79 94 109 112-113 117 122 125 138 141 154 160 162 164 172 176 186 189 192 204 214 220-221 232 238 251 255 257 273 276-278 324 326 328-331 333 335 337 341-343 347 354-355 357 367-371 374-375 379 382-386 388-392 397 399-400 404 406-408 410-411 425 431 435-436 444 451 455 457 459 461 464-465 470-471 475 479 483 485 487-488 491 501 506-508 511 513-519 523-524 526 529 531-532 534-535 537 539-540 542-545 552-554 557-560 563 566 569 572 577 580 584 587-588 590 597-598 602 604-605 609 611 613 615 624 627 631-634 637 639-640 643 648-649 654 664 669-670 672-673 676-679 681 689 691-695 697-698 706 714 731 734 737

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
induced neuron cells	Strategene	NTD001	36 57 164 284 388 397 420 481 485 501 524 528-529 539 542 545 560 571 579 582 595 602 620 637 654 667 689 730
retinoid acid induced neuronal cells	Strategene	NTR001	524 584 693
neuronal cells	Strategene	NTU001	36-38 120 204 331 351 354 357 386 388 399 411 442 459 516 533 539 545 565 586 606 615 621 637-638 642 646 648 714 730
placenta	Clontech	PLA003	503 579 690
prostate	Clontech	PRT001	15 40 65 164 187 207 229 337 348 367 375 377-378 395 406 416 428 458 468 476 511 524 526 531 534 538 555 559 563 576 584 597 613 622 624 631 642 667 672 677 684 724 734
rectum	Invitrogen	REC001	57 67 164 260 331 343 370-371 380 382 384 404 409 436 444 475 485 498 513 524 526 540 542 552 554 581 615 619 624 627 634 654 659 671 689 714
salivary gland	Clontech	SAL001	21 84 106-107 152 179 238 246 255 273 287 371 378 383 401 407 420 455 475 477 509 512 515 521 541 548 565 570-571 573-574 589 606 628 634 636 652 689 703 738
skin fibroblast	ATCC	SFB002	192
skin fibroblast	ATCC	SFB003	464
small intestine	Clontech	SIN001	57 66 71 98 116 150 164 172 327 336 343 362 367 379 388 397 401-402 417 429 433 436 496 526 528 533 590 602 620 631 634 667 678 711
skeletal muscle	Clontech	SKM001	3 57 66 101 164 172 256 266 325 379 385 449 468 485 487 518 552 554 566-567 570 582 584 590 606 611 628 631 738
spinal cord	Clontech	SPC001	10 54 57 66 75 100 102 114 144 164 175 193 199 215-216 325 334 337 367 370 380 385-386 406 411-413 419 429 466 470 486 518 526 529 531 534 574 579 585 587 590 604 620-621 631-632 634 642 644 648 659 688-689 691 693 695
adult spleen	Clontech	SPLc01	478 572
stomach	Clontech	STO001	26 90 164 218 358 369 386 468 475

Tissue Origin	RNA Source	Hyseq Library Name	SEQ ID NOS:
			485 526 532 569 576 579 581 586 603 631 634 677 682 689
thalamus	Clontech	THA002	17 31 57 66 109 127 164 217-218 262 315-316 324 330 357 369 386 388 400 406 435 456 459 464 468-469 515-516 537 540-541 556 566 574 590 611 622 631 634 644 648 656 677-678 680
thymus	Clontech	THM001	6 15 26 54 79 164 172 187 193 201 264 291 315 329 331 351 356 367 397-398 401 407 412 424 427 429 435-436 443 451 474 478 482 549 563 565 567 569 576 578 581-582 610 615 621 631-632 634 648 662 667 669 679 689 693 696
thymus	Clontech	THMc02	3-6 8 11 16 18 34 58-59 67 132 149 162 164 167 172-173 186 188-189 193 200 203 216 223 232 239 255 263 265 319-320 331 333-334 355 359 370 373 377-380 382 387-390 393 395 398-399 402 404 408 420 427 434 436 467 475-476 503 508 518 524 526 532 540 560 563 565 571-572 576-577 579 582 598 601 603 612-613 615 621 627 632 634 639 641 648 651 657 659 662 672 677-678 684-686 689 696 699 706 714-716 722 726-729 732
thyroid gland	Clontech	THR001	5 29-30 40 54 57 66 72 79 117 144 160 164 166 170 172 176 183 188-189 208-209 219 230 285-286 314 318 327 331 335 338 344 347 354 363 367 375 377-380 382 384-386 388 393 397 399 401-403 419 422 429 436 442 444 451 456 458-461 464 467-468 470 472-473 476-477 481 488 494 503 508-509 511 516 519-521 524 528-529 533 537-538 543 548 557 559-560 563 565-566 571-574 576 582 585 587 590-591 593-594 596-597 606 614-615 620-621 623-624 627 631-634 640 650-651 653 662 667 669-670 675 679 689 708 712 714
trachea	Clontech	TRC001	156 164 171 240 375 378 390 400 422 468 484 565 574 581 585 587 631 654 689 714
uterus	Clontech	UTR001	65 77 79 101 164 220 367 369 451 468 526 530 533 548 554 559 562 568 573 582 594 637 648 689

Table 2 - Nearest Neighbor Results

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
1	1000	gi7021484	Mus musculus	secretory carrier membrane protein 4	567	85
2	10017	R06463	Homo sapiens	Derived protein of clone ICA13 (ATCC 40553).	848	100
3	10020	gi1065967	Caenorhabditis elegans	similar to other protein phosphatases 1, 2A and 2B	325	36
4	10024	G03460	Homo sapiens	Human secreted protein,	439	98
5	10032	Y12505	Homo sapiens	Human 5' EST secreted protein	136	87
6	10042	Y29511	Homo sapiens	Human lung tumour protein SAL-25 1st predicted amino acid sequence.	701	100
7	1006	Y92324	Homo sapiens	Human alpha-2-delta-D polypeptide from splice variant 1.	763	100
8	10064	gi4589375	Homo sapiens	Gab2	425	58
9	1007	gi7018398	Homo sapiens		151	75
10	1008	gi896065	Homo sapiens	protein that is immuno-reactive with anti-PTH polyclonal antibodies	1226	99
11	10088	gi3779244	Homo sapiens	Metallo-protease 1	1512	98
12	10089	gi2947232	Homo sapiens	membrane associated guanylate kinase 2	523	100
13	10091	gi3347863	Mus musculus	cAMP-specific cyclic	223	54

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				nucleotide phosphodiesterase PDE8; MMPDE8		
14	10098	gi6979311	Homo sapiens	cysteine-rich repeat-containing protein S52 precursor	1068	100
15	10102	G01395	Homo sapiens	Human secreted protein,	297	88
16	10103	gi854733	Rattus norvegicus	casein kinase 1 gamma 1 isoform	293	84
17	10104	Y60017	Homo sapiens	Human endometrium tumour EST encoded protein 77.	154	100
18	10108	G03290	Homo sapiens	Human secreted protein,	215	97
19	10110	gi7292299	Drosophila melanogaster	CG1271 gene product	208	46
20	10111	gi4512334	Rattus norvegicus	Ca/calmodulin-dependent protein kinase kinase alpha, CaM-kinase kinase alpha	822	89
21	10113	Y41694	Homo sapiens	Human PRO382 protein sequence.	633	97
22	10114	gi349075	Rattus norvegicus	calmodulin-binding protein	531	99
23	10116	gi162981	Bos taurus	endozepine-related protein precursor	937	87
24	10121	gi8979743	Canis familiaris	Band4.1-like5 protein	643	100
25	10126	Y99420	Homo sapiens	Human PRO1486 (UNQ755) amino acid sequence	607	100
26	1013	gi804750	Homo sapiens	protein tyrosine	614	73

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				phosphatase		
27	10136	W02105	Homo sapiens	Human L-asparaginase.	1243	98
28	10142	Y35924	Homo sapiens	Extended human secreted protein sequence,	862	89
29	10148	gi3334982	Homo sapiens	R27216_1	329	98
30	1015	G02485	Homo sapiens	Human secreted protein,	120	72
31	10154	gi10798804	Homo sapiens	sperm antigen	2607	98
32	10175	Y96864	Homo sapiens	SEQ. ID. 37 from WO0034474.	536	100
33	10196	gi553621	Homo sapiens	profilaggrin	346	39
34	10198	gi1419016	Mus musculus	odorant receptor	281	53
35	10200	Y57903	Homo sapiens	Human transmembrane protein HTMPN-27.	448	100
36	10208	gi4062492	Escherichia coli		505	100
37	10212	gi882529	Escherichia coli	ORF_f141	625	96
38	10213	gi4062778	Escherichia coli	Hypothetical protein HI0761	773	98
39	10214	gi6693832	Rattus norvegicus	opioid growth factor receptor	661	44
40	10227	G01360	Homo sapiens	Human secreted protein,	384	100
41	10236	gi1651257	Escherichia coli	.	373	100
42	10241	gi2769262	Escherichia coli	catabolite gene activator protein	178	96
43	10245	gi1789539	Escherichia coli	orf, hypothetical protein	679	98
44	10246	gi882492	Escherichia coli	ORF_o179	488	97
45	10247	gi1742149	Escherichia coli	Sn-glycerol-3-phosphate	323	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				transport system permease protein UgpA.		
46	10282	Y29817	Homo sapiens	Human synapse related glycoprotein 2.	521	96
47	1031	gi6435130	Mus musculus	putative E1-E2 ATPase	990	86
48	1040	gi854124	Homo sapiens	Human giant larvae homologue	471	63
49	1043	gi3882285	Homo sapiens	KIAA0782 protein	154	61
50	1051	gi178216	Homo sapiens	anion exchange protein 1	172	100
51	1053	Y76748	Homo sapiens	Human protein kinase homologue, PKH-1.	180	92
52	1062	gi965014	Mus musculus	ADAM 4 protein precursor	492	65
53	1063	gi2393880	Drosophila melanogaster	A-kinase anchor protein DAKAP550	580	60
54	1066	gi2746788	Caenorhabditis elegans	contains similarity to transacylases	607	35
55	107	G00357	Homo sapiens	Human secreted protein,	183	77
56	1071	gi9105937	Xylella fastidiosa	Acetylglutamate kinase	505	36
57	1085	R95913	Homo sapiens	Neural thread protein.	257	55
58	1086	Y76332	Homo sapiens	Fragment of human secreted protein encoded by gene 38.	387	58
59	1088	gi4589642	Homo sapiens	KIAA0999 protein	873	99
60	109	gi763431	Homo sapiens	KIAA0999 protein	360	85
61	1095	Y94907	Homo sapiens	Human secreted	701	97

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				protein clone ca106_19x protein sequence		
62	1102	Y07096	Homo sapiens	Colon cancer associated antigen precursor sequence.	1982	100
63	1105	Y84907	Homo sapiens	A human proliferation and apoptosis related protein.	983	91
64	1108	gi1398903	Mus musculus	Ca2+ dependent activator protein for secretion	1307	89
65	1109	Y91524	Homo sapiens	Human secreted protein sequence encoded by gene 74	2400	99
66	1113	gi1657462	Sus scrofa	calcium/calmodulin-dependent protein kinase II isoform gamma-E	1348	94
67	1117	Y32169	Homo sapiens	Human growth-associated protease inhibitor heavy chain precursor.	2831	97
68	1118	gi3063517	Homo sapiens		1138	98
69	1125	gi8248285	Homo sapiens	sphingosine kinase type 2 isoform	1290	98
70	1132	Y94918	Homo sapiens	Human secreted protein clone dd504_18 protein sequence	437	59
71	1143	gi45806	Homo sapiens	prepro-major	209	40

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		77		basic protein homolog		
72	1146	gi182395	Homo sapiens	focal adhesion kinase	131	87
73	1161	W90962	Homo sapiens	Human CSGP-2 protein.	931	100
74	117	W69428	Homo sapiens	Human secreted protein bp537_4.	159	93
75	1170	gi34339	Homo sapiens		586	87
76	1175	gi7960243	Homo sapiens	SNARE protein kinase SNAK	308	100
77	118	gi5360093	Homo sapiens	NY-REN-18 antigen	178	96
78	1183	gi292037	Homo sapiens	helix-loop-helix phosphoprotein	361	91
79	1193	gi1899186	Rattus norvegicus	polysialyltransferase	171	76
80	1195	gi1399462	Homo sapiens	serine/threonine-protein kinase PRP4h	208	71
81	1198	gi181535	Homo sapiens	defensin precursor	150	71
82	1201	gi5668935	Rattus norvegicus	plasma membrane Ca2+ ATPase isoform 1kb	244	73
83	1207	gi6224868	Homo sapiens	TANK binding kinase TBK1	716	86
84	1210	gi179646	Homo sapiens	complement component C1s	242	61
85	1211	gi1483187	Homo sapiens		296	65
86	1214	gi7800638	Streptococcus pneumoniae	PspA	121	37
87	123	Y44810	Homo sapiens	Human Aspartic Protease-2 (NHAP-2).	218	93
88	1259	gi2116672	Homo sapiens	EAR-1r	128	70
89	1266	gi7243125	Homo sapiens	KIAA1372 protein	403	53
90	1270	gi1289445	Homo sapiens	diacylglycerol kinase epsilon DGK	125	96

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
91	1290	gi1429371	Drosophila melanogaster	ubiquitin-specific protease	470	41
92	1291	Y66755	Homo sapiens	Membrane-bound protein PRO1185.	993	100
93	1296	gi9652087	Homo sapiens	scavenger receptor cysteine-rich type 1 protein M160 precursor	1183	99
94	1299	gi7300398	Drosophila melanogaster	CG7683 gene product	397	40
95	1317	gi3695115	Rattus norvegicus	CL1AA	216	100
96	132	gi187171	Homo sapiens	12-lipoxygenase	176	97
97	1330	Y12482	Homo sapiens	Human 5' EST secreted protein	65	44
98	1336	gi10798814	Homo sapiens	MLTK-beta	2366	99
99	135	gi456090	Homo sapiens	effector cell protease receptor 1	190	74
100	1356	gi193057	Mus musculus	envelope polyprotein precursor	131	36
101	1369	gi458657	Homo sapiens	glucocorticoid receptor alpha-2	596	89
102	1392	gi8493519	Mus musculus	nuclear localization signal binding protein	145	59
103	1408	gi3127051	Rattus norvegicus	potassium channel regulatory protein KChAP	176	84
104	141	gi6453613	Mus musculus	putative protein kinase	204	33
105	1424	gi2982501	Homo sapiens	neuropathy target esterase	769	100
106	143	W50033	Homo sapiens	Human immunity related factor.	1201	98
107	1431	gi10644	Heterodera	hypothetical	133	36

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		565	glycines	esophageal gland cell secretory protein 10		
108	1441	gi3044086	Myxococcus xanthus	unknown	149	32
109	1444	gi7248381	Homo sapiens	adaptor protein p130Cas	1615	97
110	1447	Y65168	Homo sapiens	Human 5' EST related polypeptide	403	97
111	1457	W19919	Homo sapiens	Human Ksr-1 (kinase suppressor of Ras).	227	77
112	1471	G02532	Homo sapiens	Human secreted protein,	97	59
113	1473	gi6062874	Homo sapiens	candidate tumor suppressor protein DICE1	581	100
114	1474	Y64896	Homo sapiens	Human 5' EST related polypeptide	197	100
115	1483	gi436218	Homo sapiens	KIAA0037	295	76
116	1486	gi5852834	Homo sapiens	bridging integrator-2	133	64
117	149	gi3327162	Homo sapiens	KIAA0674 protein	2243	98
118	1503	gi1736785	Escherichia coli	.	1270	97
119	1506	gi4062298	Escherichia coli	YhhI protein	612	90
120	1513	gi4062346	Escherichia coli	.	556	94
121	1514	gi216609	Escherichia coli	PhoQ protein	661	90
122	1523	gi5712756	Rattus norvegicus	calcium transporter CaT1	1178	90
123	1527	gi1853980	Mus musculus	glucocorticoid receptor interacting protein 1	171	84
124	1536	Y17227	Homo sapiens	Human secreted	452	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				protein (clone ya1-1).		
125	154	gi8515090	Pinus taeda	putative arabinogalactan protein	81	40
126	1544	gi3879933	Caenorhabditis elegans	Similarity to Xenopus F-spondin precursor (PIR Acc. No. comes from this gene	134	34
127	1554	gi6523817	Homo sapiens	SIR protein	255	84
128	1555	gi6635205	Homo sapiens	beta-ureidopropionase	210	90
129	1556	Y39286	Homo sapiens	Phosphodiesterase 10 (PDE10) clone FB93a.	161	61
130	1564	gi8977945	Streptomyces coelicolor A3(2)	putative secreted serine protease	231	45
131	1576	gi3025828	Rattus norvegicus	signal transducer and activator of transcription 4	183	97
132	1578	gi5106572	Homo sapiens	transcriptional activator SRCAP	758	98
133	1579	gi8575527	Homo sapiens	toll-like receptor 8	595	99
134	158	gi406058	Mus musculus	protein kinase	168	70
135	1580	gi63340	Gallus gallus	c-Rmil	231	90
136	1588	gi2217931	Homo sapiens	PKU-alpha	127	92
137	1589	gi1272422	Mus musculus	Phosphoinositide 3-kinase	720	99
138	159	gi2224629	Homo sapiens	KIAA0344	215	43
139	1600	gi1016012	Rattus norvegicus	neural cell adhesion protein BIG-2 precursor	543	93
140	161	gi6649583	Homo sapiens	kidney and liver proline	1651	98

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				oxidase 1		
141	1612	gi406113	Rattus norvegicus	protein kinase I	125	89
142	1615	gi219992	Homo sapiens	phSR2	150	78
143	1620	gi5714636	Homo sapiens	serine/threonine protein kinase Kp78 splice variant CTAK75a	126	71
144	1644	Y13352	Homo sapiens	Amino acid sequence of protein PRO228.	2542	100
145	1647	Y99444	Homo sapiens	Human PRO1575 (UNQ781) amino acid sequence	704	100
146	1650	gi3789765	Homo sapiens	transmembrane receptor UNC5C	271	100
147	1663	W75258	Homo sapiens	Fragment of human secreted protein encoded by gene 26.	163	96
148	1665	gi10432431	Homo sapiens	secreted modular calcium-binding protein	1428	99
149	1671	gi6708169	Mus musculus	inositol phosphatase eSHIPD183	169	97
150	1672	Y68773	Homo sapiens	Amino acid sequence of a human phosphorylation effector PHSP-5.	1030	99
151	1678	gi6063017	Homo sapiens	tousled-like kinase 1	132	86
152	1680	gi3510603	Homo sapiens	nuclear receptor co-repressor N-CoR	278	80
153	1692	gi1546084	Homo sapiens	farnesol receptor HRR-1	165	100
154	1698	gi520469	Oryctolagus cuniculus	597 aa protein related to	177	94

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				Na/glucose cotransporters		
155	1702	gi10432382	Homo sapiens		519	95
156	1704	Y91668	Homo sapiens	Human secreted protein sequence encoded by gene 73	214	75
157	1708	gi3080757	Mus musculus	growth factor independence-1B	457	78
158	1716	gi29653	Homo sapiens	putative oncogene	220	92
159	173	gi3452473	Rattus norvegicus	serine/threonine protein kinase TAO1	699	100
160	1731	Y27581	Homo sapiens	Human secreted protein encoded by gene No. 15.	774	100
161	1732	gi9652087	Homo sapiens	scavenger receptor cysteine-rich type 1 protein M160 precursor	1025	98
162	174	Y35923	Homo sapiens	Extended human secreted protein sequence,	1691	100
163	1740	Y53014	Homo sapiens	Human secreted protein clone fn189_13 protein sequence	337	60
164	1748	gi7770237	Homo sapiens	PRO2822	218	93
165	1751	gi8979825	Homo sapiens		306	50
166	1755	R95332	Homo sapiens	Tumor necrosis factor receptor 1 death domain ligand (clone	1184	62

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				3TW).		
167	1762	gi7380947	Homo sapiens	Gem-interacting protein	1545	99
168	1776	gi5912265	Homo sapiens	hypothetical protein	224	100
169	1777	Y70461	Homo sapiens	Human membrane channel protein-11 (MECHP-11).	413	95
170	1781	R26060	Homo sapiens	Growth Factor Receptor Bound protein GRB-1.	398	98
171	1796	gi10312169	Homo sapiens	serine carboxypeptidase 1 precursor protein	1381	99
172	180	gi3002527	Homo sapiens	neuronal thread protein AD7c-NTP	477	61
173	182	gi7385131	Homo sapiens	HBV pX associated protein-8; XAP-8	2066	82
174	1820	G03249	Homo sapiens	Human secreted protein,	370	97
175	1822	gi473969	Oryctolagus cuniculus	one of the members of sodium-glucose cotransporter family	1048	90
176	1829	gi10440355	Homo sapiens	FLJ00012 protein	310	96
177	1832	gi165650	Oryctolagus cuniculus	phosphorylase kinase beta-subunit	146	96
178	1834	W75132	Homo sapiens	Human secreted protein encoded by gene 11 clone HCENJ40.	423	47
179	1837	gi60369	Saimiriine herpesvirus 2	ORF 48~EDLF5~sim. to EBV BRRF2	615	71

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
180	1859	gi9989696	Homo sapiens	ROR2 protein	645	87
181	1880	gi7340847	Mus musculus	chondroItin 4-sulfotransferase	275	40
182	1881	gi7573291	Homo sapiens		298	100
183	1890	gi3149950	Homo sapiens	ST1C2	183	94
184	1899	gi2143260	Homo sapiens	Phosphoino-sitide 3-kinase	346	98
185	19	gi1808582	Homo sapiens	U2AF1-RS2	224	46
186	192	G03192	Homo sapiens	Human secreted protein,	267	86
187	1922	gi485858	Mus musculus	IB3/5-polypeptide	1206	78
188	1945	gi37261	Homo sapiens		1402	97
189	195	W67863	Homo sapiens	Human secreted protein encoded by gene 57 clone HFEBF41.	551	98
190	1957	gi406738	Homo sapiens	Shb	263	44
191	1969	Y41701	Homo sapiens	Human PRO708 protein sequence.	975	98
192	1970	gi3979817	Caenorhabditis elegans	Weak similarity to Human tyrosine-protein kinase CSK	254	49
193	1973	G00796	Homo sapiens	Human secreted protein,	365	98
194	1985	gi4558637	Homo sapiens	Putative homolog of hypoxia inducible factor three alpha	1420	99
195	1986	gi4455015	Homo sapiens	host cell factor homolog	367	50

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				LCP		
196	2	G02532	Homo sapiens	Human secreted protein,	106	85
197	2004	gi10503935	Homo sapiens	type A calpain-like protease	961	100
198	2023	gi1651341	Escherichia coli	.	1075	97
199	2025	Y71069	Homo sapiens	Human membrane transport protein, MTRP-14.	540	100
200	2038	gi8572543	Homo sapiens	membrane-associated lectin type-C	686	98
201	2041	gi37400	Homo sapiens	trk-2h polypeptide	228	89
202	2043	W75096	Homo sapiens	Human secreted protein encoded by gene 40 clone HNEDJ57.	290	38
203	2068	G03394	Homo sapiens	Human secreted protein,	595	97
204	2072	gi2116552	Rattus norvegicus	cationic amino acid transporter 3	1025	85
205	2076	gi157409	Drosophila melanogaster	fat protein	369	39
206	2078	gi1054940	Gallus gallus	cSH-PTP2	605	94
207	2084	gi9663128	Homo sapiens	hypothetical protein	874	99
208	2088	gi10567590	Homo sapiens	sodium bicarbonate cotransporter-like protein	609	100
209	2089	gi1789001	Escherichia coli	putative ATP-binding component of a transport system	961	98
210	2097	Y70460	Homo sapiens	Human membrane channel	258	96

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				protein-10 (MECHP-10).		
211	2108	gi3207508	Rattus norvegicus	hexokinase	767	74
212	2111	gi6330233	Homo sapiens	KIAA1176 protein	3710	99
213	2118	W74797	Homo sapiens	Human secreted protein encoded by gene 68 clone HKIXR69.	156	96
214	2134	gi1780991	Homo sapiens	branched chain acyl-CoA oxidase	209	97
215	2146	gi7688148	Homo sapiens	hypothetical protein	1038	100
216	2149	gi2280485	Homo sapiens	KIAA0376	917	100
217	2153	gi1842429	Rattus norvegicus	ankyrin binding cell adhesion molecule neurofascin	592	88
218	2155	gi6526791	Homo sapiens	Eps15R	1126	100
219	2161	gi7300427	Drosophila melanogaster	CG7709 gene product	200	33
220	2163	Y52296	Homo sapiens	Human isomerase homologue-3 (HIH-3).	186	91
221	2173	W34526	Homo sapiens	hTCP protein fragment.	164	93
222	2178	gi3360512	Rattus norvegicus	Citron-K kinase	299	94
223	2180	Y74008	Homo sapiens	Human prostate tumor EST fragment derived protein #195.	261	41
224	2184	gi53041	Mus musculus		130	41
225	2186	gi4017774	Homo sapiens	ribosomal protein S6 kinase 3	142	64
226	2190	gi5772955	Homo sapiens	The ha1225 gene product is related to human alpha-	176	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				glucosidase.		
227	2210	gi2055392	Rattus norvegicus	transmembrane receptor UNC5H1	620	90
228	2214	gi7861733	Homo sapiens	low density lipoprotein receptor related protein-deleted in tumor	1360	98
229	2223	gi7959189	Homo sapiens	KIAA1464 protein	884	99
230	223	W88627	Homo sapiens	Secreted protein encoded by gene 94 clone HPMBQ32.	300	77
231	2233	gi7839587	Homo sapiens	organic anion transporting polypeptide 14	1092	99
232	2237	gi10440400	Homo sapiens	FLJ00033 protein	1212	99
233	2251	gi5923786	Homo sapiens	zinc metallo-protease ADAMTS6	277	44
234	2256	W63698	Homo sapiens	Human secreted protein 18.	516	100
235	2259	gi4678722	Homo sapiens	hypothetical protein	387	36
236	2262	Y33741	Homo sapiens	Beta-secretase.	793	99
237	2265	gi7018545	Homo sapiens	hypothetical protein	608	94
238	2271	gi4186183	Homo sapiens	unknown	684	53
239	2273	gi7243035	Homo sapiens	KIAA1327 protein	1031	100
240	2280	gi5809678	Homo sapiens	sperm membrane protein BS-63	342	95
241	2286	gi6224691	Homo sapiens	Na+/sulfate cotransporter SUT-1	1221	99
242	2291	gi207621	Rattus norvegicus	uromodulin	345	50
243	2292	gi7296304	Drosophila melanogaster	CG5274 gene product	272	35
244	2294	Y28503	Homo sapiens	HGFH3 Human Growth Factor	320	98

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				Homologue 3.		
245	2296	W88799	Homo sapiens	Polypeptide fragment encoded by gene 45.	223	86
246	2303	gi7110160	Homo sapiens	guanine nucleotide exchange factor	1212	99
247	2306	gi6434874	Mus musculus	calcium/calmodulin dependent protein kinase kinase alpha	576	84
248	2309	Y95433	Homo sapiens	Human calcium channel SOC-2/CRAC-1 C-terminal polypeptide.	1203	99
249	2313	gi7300943	Drosophila melanogaster	CG4677 gene product	689	79
250	2318	W48351	Homo sapiens	Human breast cancer related protein BCRB2.	202	59
251	2329	G01772	Homo sapiens	Human secreted protein,	311	84
252	2330	Y41729	Homo sapiens	Human PRO1071 protein sequence.	886	99
253	2342	gi3786430	Caenorhabditis elegans		268	42
254	2350	gi930104	Homo sapiens	protein-tyrosine phosphatase	571	79
255	2359	gi9392591	Homo sapiens	CC chemokine CCL28	679	99
256	2361	gi1666689	Mus musculus	alpha-NAC, muscle-specific form gp220	357	41
257	2374	G03172	Homo sapiens	Human secreted protein,	112	78
258	2387	gi1399197	Homo sapiens	pyruvate dehydrogenase kinase isoform 4	201	85
259	2401	G01757	Homo sapiens	Human	612	99

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				secreted protein,		
260	2409	gi181123	Homo sapiens	cleavage signal 1 protein	194	86
261	2431	gi7018547	Homo sapiens	hypothetical protein	473	50
262	2432	gi4826496	Homo sapiens		327	39
263	2467	G03667	Homo sapiens	Human secreted protein,	640	97
264	2471	gi7688148	Homo sapiens	hypothetical protein	1284	91
265	2478	gi790819	Homo sapiens	polycystic kidney disease-associated protein	615	90
266	2484	gi3327080	Homo sapiens	KIAA0633 protein	1747	99
267	249	G03793	Homo sapiens	Human secreted protein,	139	65
268	2490	gi6467371	Homo sapiens	thyrotropin-releasing hormone degrading ectoenzyme	757	98
269	25	G03203	Homo sapiens	Human secreted protein,	137	65
270	2504	gi4097712	Homo sapiens	HBV associated factor	166	74
271	2506	gi2072784	Homo sapiens	Na+/nucleoside cotransporter	201	95
272	2507	gi5924007	Homo sapiens		335	38
273	2510	gi7717385	Homo sapiens	beta-site APP-cleaving enzyme 2, EC 3.4.23.	383	89
274	2523	gi339709	Homo sapiens		150	96
275	253	gi36615	Homo sapiens	serine/threonine protein kinase	391	77
276	2533	gi45896	Homo sapiens	KIAA0985	191	61

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		14		protein		
277	2536	gi2088685	Caenorhabditis elegans	strong similarity to the CDC2/CDX subfamily of ser/thr protein kinases	419	55
278	2544	gi1002425	Mus musculus	YSPL-1 form 2	280	80
279	2568	Y41738	Homo sapiens	Human PRO541 protein sequence.	379	49
280	2580	gi3004482	Rattus norvegicus	putative integral membrane transport protein	382	49
281	2593	gi7300049	Drosophila melanogaster	CG4525 gene product	582	50
282	2600	gi4530437	Homo sapiens	thyroid hormone receptor-associated protein complex component TRAP240	334	90
283	2625	gi8099652	Homo sapiens	toll-like receptor 9 form A	761	96
284	2641	gi148019	Escherichia coli	tolA	692	100
285	2667	gi1750387	Pseudomonas aeruginosa	Carbamoyl-phosphate synthetase large subunit	143	76
286	2670	gi4883437	Mus musculus	RNA binding protein	139	92
287	2673	Y66656	Homo sapiens	Membrane-bound protein PRO943.	1869	98
288	2676	gi3885978	Mus musculus	mismatch-specific thymine-DNA glycosylate	123	88
289	2680	gi6453438	Homo sapiens	hypothetical protein	465	82
290	2682	gi18417	Mus musculus	GATA-5	527	77

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		56		cardiac transcription factor		
291	2684	gi9844920	Homo sapiens	nicotinic acetylcholine receptor subunit alpha 10	294	88
292	2695	gi1789764	Escherichia coli	putative transport	879	98
293	2697	gi349229	Escherichia coli	peripheral membrane protein	936	99
294	2698	gi4062194	Escherichia coli	.	737	100
295	2700	gi529240	Escherichia coli	homoserine kinase	578	100
296	2704	gi1552831	Escherichia coli	hypothetical	420	100
297	2712	gi1789672	Escherichia coli	putative ATP-binding component of a transport system	262	100
298	2716	gi4062409	Escherichia coli	Transmembrane protein dppC	382	100
299	2719	gi304976	Escherichia coli	matches PS00017: ATP_GTP_A and PS00301: EFACTOR_GTP; similar	921	95
300	2724	gi145856	Escherichia coli	nmpC	647	97
301	2725	gi1789473	Escherichia coli	putative transport protein	312	100
302	2728	gi1805561	Escherichia coli		222	97
303	2729	gi43248	Escherichia coli		655	91
304	2744	gi396299	Escherichia coli	similar to E. coli pyruvate formate-lyase activating enzyme	675	100
305	2749	gi1742648	Escherichia coli	.	592	100
306	2752	gi40622	Escherichia	Sensor kinase	357	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		36	coli	CitA		
307	2762	gi1787795	Escherichia coli	putative LACI-type transcriptional regulator	342	100
308	2764	gi1799743	Escherichia coli	putative LACI-type transcriptional regulator	151	84
309	2768	gi405964	Escherichia coli	yohG	534	94
310	2774	gi4062338	Escherichia coli	.	387	97
311	2790	gi4062338	Escherichia coli	.	420	86
312	2800	gi1789805	Escherichia coli	putative transport	572	100
313	2811	gi5305333	Mus musculus	protein kinase Myak-S	421	49
314	2827	gi10047251	Homo sapiens	KIAA1588 protein	531	97
315	2830	G02872	Homo sapiens	Human secreted protein,	185	62
316	2836	gi191175	Cricetulus sp.	cAMP-dependent protein kinase alpha-catalytic subunit	1677	97
317	2851	gi558846	Homo sapiens	BCL2/adeno-virus E1B 19kD-interacting protein 3	220	61
318	2856	gi3882211	Homo sapiens	KIAA0745 protein	232	93
319	2866	gi6329708	Homo sapiens	KIAA1119 protein	1331	91
320	2874	gi2853033	Mus musculus	tousled-like kinase	203	82
321	2882	gi10185134	Schizosaccharomyces pombe	hypothetical zinc-finger protein	318	42
322	2886	G03797	Homo sapiens	Human secreted protein,	140	69
323	2899	gi4240325	Homo sapiens	KIAA0918 protein	170	53

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
324	2906	Y94988	Homo sapiens	Human secreted protein vl1_1,	1738	100
325	2920	gi9453735	Homo sapiens		1926	100
326	2925	gi6434876	Homo sapiens	CDK4-binding protein p34SEI1	1210	100
327	2930	gi3941320	Schistosoma japonicum	myosin	208	28
328	2934	Y31645	Homo sapiens	Human transport-associated protein-7 (TRANP-7).	642	63
329	2955	G01165	Homo sapiens	Human secreted protein,	528	99
330	2967	gi7263960	Homo sapiens		466	100
331	2980	gi4589530	Homo sapiens	KIAA0943 protein	1849	94
332	2994	G03812	Homo sapiens	Human secreted protein,	124	61
333	2996	gi9857400	Homo sapiens	tumor endothelial marker 1 precursor	2666	98
334	2999	Y66697	Homo sapiens	Membrane-bound protein PRO1383.	2254	100
335	3	gi6289072	Homo sapiens	JM24 protein	930	100
336	3008	Y45219	Homo sapiens	Human CASB47 protein.	557	92
337	3013	gi5262678	Homo sapiens	hypothetical protein	1747	100
338	3041	Y73335	Homo sapiens	HTRM clone 1850120 protein sequence.	1315	99
339	306	gi4868443	Mesocricetus auratus	Mx-interacting protein kinase PKM	1867	95
340	3061	gi433338	Homo sapiens	protein-tyrosine kinase	3934	94

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
341	309	Y76145	Homo sapiens	Human secreted protein encoded by gene 22.	1313	99
342	3095	gi7300159	Drosophila melanogaster	CG14899 gene product	190	57
343	3098	gi532056	Homo sapiens	protein-tyrosine-phosphatase	2641	86
344	3105	gi285987	Homo sapiens	mitochondrial outer membrane protein 19	192	71
345	3118	gi9929935	Macaca fascicularis	hypothetical protein	180	61
346	3124	gi8131903	Mus musculus	transient receptor potential-related protein	226	100
347	3126	Y02370	Homo sapiens	Polypeptide identified by the signal sequence trap method.	261	100
348	3166	gi7290860	Drosophila melanogaster	CG1531 gene product	534	42
349	3175	gi6649583	Homo sapiens	kidney and liver proline oxidase 1	1752	95
350	3176	gi7208438	Homo sapiens	long-chain 2-hydroxy acid oxidase HAOX2	1048	95
351	3188	Y02693	Homo sapiens	Human secreted protein encoded by gene 44 clone HTDAD22.	243	57
352	3191	gi7105926	Homo sapiens	calcium channel alpha2-delta3 subunit	300	96
353	3208	gi10334774	Homo sapiens	MUCDHL-FL	613	98
354	3226	Y87209	Homo sapiens	Human secreted protein sequence	3147	99

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
355	3235	gi6715135	Homo sapiens	Fanconi anemia, complementation group F	1947	99
356	3257	gi5441615	Canis familiaris	zinc finger protein	326	42
357	3282	G03002	Homo sapiens	Human secreted protein,	211	61
358	3289	gi3288457	Homo sapiens	PI3-kinase	5832	97
359	3296	gi7770139	Homo sapiens	PRO1722	293	64
360	3298	gi2198815	Ambystoma tigrinum	electrogenic Na+ bicarbonate cotransporter; NBC	1278	52
361	3303	gi4028015	Homo sapiens	potassium channel	1881	92
362	3305	gi5902966	Homo sapiens	very large G-protein coupled receptor-1	1770	100
363	3308	gi219944	Homo sapiens	The first in-frame ATG codon is located at nucleotides NPPase.	3967	86
364	3325	gi3510234	Homo sapiens	R31237_1, partial CDS	192	94
365	3341	W78899	Homo sapiens	Human UNC-5 homologue UNC5H-1.	1614	90
366	3342	gi1478205	Mus musculus	PNG protein	341	70
367	3350	gi2739460	Bos taurus	regulator of G-protein signaling 7	2263	98
368	3372	gi7671663	Homo sapiens		375	79
369	338	Y84322	Homo sapiens	A human cardiovascular system associated protein kinase-3.	2606	100
370	3383	gi10441	Homo sapiens	protein	1127	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		382		kinase		
371	3395	gi530823	Homo sapiens	epidermal growth factor receptor kinase substrate	402	47
372	3405	Y29332	Homo sapiens	Human secreted protein clone pe584_2 protein sequence.	1220	94
373	3408	gi3334741	Homo sapiens	shal-type potassium channel	2888	90
374	345	gi4539527	Homo sapiens	NAALADase L protein	600	72
375	346	Y95434	Homo sapiens	Human calcium channel SOC-3/CRAC-2 C-terminal polypeptide.	1802	99
376	3470	gi9798452	Homo sapiens	putative capacitative calcium channel	277	100
377	3482	gi3818572	Homo sapiens	cAMP-specific phosphodiesterase 8B; PDE8B1; 3',5'-cyclic nucleotide phosphodiesterase	2353	96
378	3492	gi1665825	Homo sapiens		3878	99
379	3530	gi505100	Homo sapiens	KIAA0066	3637	100
380	3533	Y32169	Homo sapiens	Human growth-associated protease inhibitor heavy chain precursor.	2860	99
381	3545	gi6624133	Homo sapiens		449	98
382	3549	gi1469193	Homo sapiens	The KIAA0135 gene is related to	5374	99

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				pim-1 oncogene.		
383	3595	gi6330190	Homo sapiens	KIAA1169 protein	1893	100
384	3601	gi808915	Homo sapiens	tumor necrosis factor receptor type 1 associated protein	992	99
385	3612	gi5305448	Mus musculus	SH2-B PH domain containing signaling mediator 1 gamma isoform	1439	92
386	3613	Y32194	Homo sapiens	Human receptor molecule (REC) encoded by Incyte clone 266775.	1438	100
387	3621	gi897849	Mus musculus	ubiquitinating enzyme E2-230 kDa	393	68
388	3624	R47858	Homo sapiens	Human LDL receptor Domains 1 and 2.	2895	100
389	3625	Y57949	Homo sapiens	Human transmembrane protein HTMPN-73.	1868	100
390	3626	W69342	Homo sapiens	Secreted protein of clone CJ424_9.	442	94
391	3627	gi6537136	Homo sapiens	putative organic anion transporter	982	92
392	3630	Y06886	Homo sapiens	HWHHJ20 polypeptide.	1109	91
393	3642	gi4886467	Homo sapiens	hypothetical protein	570	52
394	3645	gi9588402	Homo sapiens		598	98
395	3647	Y12050	Homo sapiens	Human 5' EST secreted protein	517	98

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
396	3653	Y70018	Homo sapiens	Human Protease and associated protein-12 (PPRG-12).	2232	99
397	3676	W67818	Homo sapiens	Human secreted protein encoded by gene 12 clone HMSJJ74.	338	100
398	3677	gi32093	Homo sapiens	HGMP07J	650	52
399	3681	Y48443	Homo sapiens	Human prostate cancer-associated protein 140.	803	93
400	3682	gi4691726	Homo sapiens	ARF GTPase-activating protein GIT1	2435	91
401	3688	gi6693824	Homo sapiens	ubiquitin-specific protease	1995	99
402	3689	Y94927	Homo sapiens	Human secreted protein clone ck213_12 protein sequence	530	81
403	3690	gi1871612	Oryctolagus cuniculus	ryanodine receptor	594	95
404	3706	gi6002714	Homo sapiens	membrane-type serine protease 1	2630	94
405	3714	gi2695708	Homo sapiens	SPOP	553	81
406	3720	gi9309293	Homo sapiens	asc-type amino acid transporter 1	566	95
407	3726	gi10440381	Homo sapiens	FLJ00026 protein	1023	69
408	373	gi5714696	Mus musculus	alpha 2 delta calcium channel subunit	243	95
409	3788	gi6911219	Homo sapiens	type II membrane serine protease	841	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
410	3789	Y45023	Homo sapiens	Human sensory transduction G-protein coupled receptor-B3.	1084	95
411	3790	gi1524088	Homo sapiens	Polio virus receptor protein	1508	99
412	3801	gi6723675	Homo sapiens	mitotic kinase-like protein-1	2035	99
413	3803	gi968973	Homo sapiens	mitotic kinase-like protein-1	332	86
414	3820	gi1770478	Homo sapiens	NK receptor	1988	99
415	3831	gi2781386	Homo sapiens		1493	99
416	3837	gi9367840	Homo sapiens	neuronal apoptosis inhibitory protein 2	2243	99
417	385	gi1526978	Homo sapiens	ryanodine receptor 2	149	96
418	3856	gi995654	Homo sapiens	interleukin-11 receptor	147	100
419	386	gi4960038	Mus musculus	T2K protein kinase homolog	669	66
420	3861	Y74129	Homo sapiens	Human prostate tumor EST fragment derived protein #316.	842	98
421	3883	gi6635205	Homo sapiens	beta-ureidopropionase	1576	100
422	3898	gi37231	Homo sapiens	DNA topoisomerase II	8436	99
423	3921	gi8648881	Homo sapiens	putative organic anion transporter	131	100
424	3932	gi8575775	Homo sapiens	KRAB zinc finger protein	1935	99
425	3934	gi4689128	Homo sapiens	SIH003	127	92
426	3963	gi3212996	Homo sapiens		339	64
427	3974	G03790	Homo sapiens	Human	232	63

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				secreted protein,		
428	3983	gi181971	Homo sapiens	vascular endothelial growth factor	433	85
429	3999	gi1657464	Sus scrofa	calcium/calmodulin-dependent protein kinase II isoform gamma-G	484	75
430	4001	gi6572230	Homo sapiens		329	100
431	4009	gi2143260	Homo sapiens	phosphoinositide 3-kinase	521	99
432	401	gi6572379	Homo sapiens		1372	56
433	4020	gi2815624	Homo sapiens	tumor necrosis factor superfamily member LIGHT	1252	100
434	4024	Y21166	Homo sapiens	Human bcl2 proto-oncogene mutant protein fragment 14.	84	40
435	4040	Y57285	Homo sapiens	Human GPCR protein (HGPRP) sequence (clone ID 2214673).	1726	99
436	4057	W74873	Homo sapiens	Human secreted protein encoded by gene 145 clone HFXHL79.	531	100
437	4066	G03714	Homo sapiens	Human secreted protein,	92	70
438	4067	gi8331760	Homo sapiens	LU1 protein	1077	92
439	4078	Y57900	Homo sapiens	Human transmembrane protein HTMPN-24.	996	100
440	4120	gi18715	Homo sapiens	mitogen-	927	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		39		activated protein kinase phosphatase 4		
441	4123	gi5360125	Homo sapiens	NY-REN-58 antigen	140	100
442	4130	gi6289072	Homo sapiens	JM24 protein	604	100
443	4133	gi8575527	Homo sapiens	toll-like receptor 8	755	100
444	4166	gi6118555	Homo sapiens	DEAD-box protein abstrakt	2512	100
445	4167	gi3800830	Rattus norvegicus	putative four repeat ion channel	615	93
446	4172	gi7209676	Homo sapiens	potassium channel Kv8.1	369	100
447	4185	gi5305405	Homo sapiens	Na+/H+ exchanger isoform 2	1769	100
448	4197	gi2811122	Xenopus laevis	NaDC-2	524	69
449	4203	Q89840_aa1	Homo sapiens	Human death associated protein DAP-3.	198	97
450	4262	gi5901478	Marmota marmota	olfactory receptor	209	92
451	4276	gi32456	Homo sapiens	protein-tyrosine phosphatase	3270	99
452	4283	R41231	Homo sapiens	GAT-2 transporter gene.	477	100
453	4331	gi3171912	Homo sapiens	RAMP2	443	98
454	4340	gi8118223	Homo sapiens	unknown	1330	100
455	4351	gi1754515	Rattus norvegicus	aminopeptidase-B	2050	92
456	4354	Y57906	Homo sapiens	Human transmembrane protein HTMPN-30.	1402	100
457	4385	gi5596433	Homo sapiens	candidate tumor suppressor protein NOC2	509	97

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
458	4388	W78140	Homo sapiens	Human secreted protein encoded by gene 15 clone HSDES04.	100	94
459	4405	Y48226	Homo sapiens	Human prostate cancer-associated protein 12.	1246	99
460	441	gi291536	Bovine herpesvirus 1	BICP4	106	35
461	4417	gi6562533	Homo sapiens	sialin	939	100
462	4419	gi1841555	Homo sapiens	NG5	146	33
463	4443	gi496139	Mus musculus	AMPA selective glutamate receptor	262	94
464	4470	gi7248381	Homo sapiens	adaptor protein p130Cas	2592	100
465	4482	gi7329979	Homo sapiens	apoptosis regulator	2071	100
466	4487	gi6706659	Homo sapiens		405	100
467	4491	gi9837341	Homo sapiens	CamKI-like protein kinase	1044	100
468	4492	Y42751	Homo sapiens	Human calcium binding protein 2 (CaBP-2).	586	99
469	4497	gi6179740	Homo sapiens	paraneoplastic cancer-testis-brain antigen	352	37
470	4502	gi6329742	Homo sapiens	KIAA1124 protein	327	100
471	4519	Y99426	Homo sapiens	Human PRO1604 (UNQ785) amino acid sequence	1563	100
472	4526	Y08008	Homo sapiens	Human HLIG-1 protein.	4023	99
473	4547	gi4589562	Homo sapiens	KIAA0959 protein	4165	99
474	4554	gi1381029	Mus musculus		1164	77

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
475	4555	gi12792366	Homo sapiens	unknown protein IT12	4461	99
476	457	Y70551	Homo sapiens	Human latent transforming growth factor-beta binding protein 3 (I).	1825	100
477	4571	gi15360115	Homo sapiens	NY-REN-45 antigen	869	100
478	4613	Y05868	Homo sapiens	Human Toll protein PRO358.	2413	100
479	4614	Y27129	Homo sapiens	Human bone marrow-derived polypeptide (clone OAF038-Leu).	1815	100
480	4622	G03789	Homo sapiens	Human secreted protein,	173	53
481	4667	gi17673638	Danio rerio	Dedd1	446	48
482	4670	gi4026409	Homo sapiens	c-rel	2309	100
483	4683	Y68773	Homo sapiens	Amino acid sequence of a human phosphorylation effector PHSP-5.	2234	99
484	4698	Y73470	Homo sapiens	Human secreted protein clone yd141_1 protein sequence	746	100
485	4724	gi6456846	Homo sapiens	hypothetical protein	1101	99
486	4734	gi3334982	Homo sapiens	R27216_1	1151	80
487	4814	gi6274473	Homo sapiens	pregnancy-induced growth inhibitor	1348	100
488	4819	Y07825	Homo sapiens	Human secreted protein fragment #4 encoded from	117	67

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				gene 28.		
489	4821	Y81498	Homo sapiens	Human foetal bone-derived growth factor-like protein.	1200	100
490	4851	gi5689491	Homo sapiens	KIAA1077 protein	4364	99
491	4872	gi5911953	Homo sapiens	hypothetical protein	3723	99
492	4902	B08917	Homo sapiens	Human secreted protein sequence encoded by gene 27	717	100
493	5006	gi435774	Homo sapiens	receptor tyrosine kinase isoform FLT4 long, FLT41 {C-terminal}	385	100
494	5007	Y93951	Homo sapiens	Amino acid sequence of a Brainiac-5 polypeptide.	804	100
495	5027	gi3548791	Homo sapiens	R33590_1	1606	100
496	5029	gi5689527	Homo sapiens	KIAA1095 protein	5722	99
497	5033	Y14482	Homo sapiens	Fragment of human secreted protein encoded by gene 17.	166	66
498	5040	Y95019	Homo sapiens	Human secreted protein vq1_1,	258	92
499	5061	gi1304434	Pseudorabies virus	EP0	85	38
500	5081	gi4038081	Homo sapiens	vascular endothelial cell growth inhibitor	134	100
501	5129	gi3169158	Homo sapiens	BC269730_2	2340	99
502	5139	gi4062856	Homo sapiens	HEXIM1 protein	293	47
503	5174	gi93685	Homo sapiens	140up gene	576	90

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		40		product		
504	524	G00329	Homo sapiens	Human secreted protein,	565	100
505	5291	Y92515	Homo sapiens	Human OXRE-12.	1271	98
506	5335	gi7296158	Drosophila melanogaster	CG3862 gene product	753	46
507	5346	Y94987	Homo sapiens	Human secreted protein vj1_1,	849	100
508	5379	gi7144506	Homo sapiens	cytokine-inducible SH2-containing protein	1353	99
509	5441	gi8096551	Homo sapiens	similar to mouse Ehm2	1516	100
510	549	Y22113	Homo sapiens	Human ZSMF-3 protein sequence.	294	62
511	5542	Y76267	Homo sapiens	Fragment of human secreted protein encoded by gene 11.	1066	100
512	5560	G03790	Homo sapiens	Human secreted protein,	103	36
513	5696	gi7920398	Homo sapiens	PTOV1	1904	91
514	5704	B08930	Homo sapiens	Human secreted protein sequence encoded by gene 2	987	100
515	5758	W18878	Homo sapiens	Human protein kinase C inhibitor, IPKC-1.	368	100
516	5760	gi6562176	Homo sapiens	hypothetical protein	425	100
517	5763	Y41706	Homo sapiens	Human PRO381 protein sequence.	441	100
518	5787	Y57907	Homo sapiens	Human transmembrane protein HTMPN-31.	952	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
519	5823	gi9800242	rat cytomegalovirus Maastricht	pr5	153	36
520	5886	gi1781037	Mus musculus	neuronal tyrosine threonine phosphatase 1	1135	52
521	5924	W69221	Homo sapiens	Human parotid secretory protein.	710	96
522	5960	Y91529	Homo sapiens	Human secreted protein sequence encoded by gene 79	1300	99
523	5962	W69784	Homo sapiens	Protein Kinase C Inhibitor-like Protein (IPKC-2).	395	100
524	5969	Y79141	Homo sapiens	Human haemopoietic stem cell regulatory protein SCM113.	1205	79
525	5976	gi780310	Homo sapiens	natural killer associated transcript 4	1808	91
526	6002	gi2104553	Homo sapiens		4367	67
527	6008	Y66765	Homo sapiens	Membrane-bound protein PRO1384.	822	100
528	6020	gi1911548	Homo sapiens	cytochrome c-like polypeptide	322	50
529	6036	W71362	Homo sapiens	Human cytokine/steroid receptor protein.	353	51
530	6070	Y42750	Homo sapiens	Human calcium binding protein 1 (CaBP-1).	626	100
531	6075	gi10732648	Homo sapiens	angiopoietin-like protein	2164	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				PP1158		
532	6106	gi2217970	Homo sapiens	p40	1349	96
533	6420	W82000	Homo sapiens	Human adult brain secreted protein dm26_2.	929	100
534	6434	gi10732648	Homo sapiens	angiopoietin-like protein PP1158	2164	100
535	6439	gi189701	Homo sapiens	endothelial cell growth factor	376	100
536	6463	Y41720	Homo sapiens	Human PRO792 protein sequence.	360	82
537	6466	gi4884084	Homo sapiens	hypothetical protein	538	100
538	6508	gi5442030	Homo sapiens	aminopeptidase	2317	96
539	6570	gi5921491	Homo sapiens		1591	99
540	6719	gi31847	Homo sapiens	glypican	1625	87
541	6772	Y65432	Homo sapiens	Human 5' EST related polypeptide	180	53
542	6789	gi537292	Homo sapiens	ICH-1L	1556	100
543	6805	gi4454702	Homo sapiens	HSPC007	634	84
544	6833	gi1890660	Homo sapiens	protein tyrosine phosphatase receptor omicron	5726	87
545	6834	gi5921491	Homo sapiens		1746	88
546	6851	gi2407641	Homo sapiens	neuropilin	3968	98
547	6868	gi6714641	Drosophila melanogaster	MAP kinase phosphatase	218	49
548	6876	Y13138	Homo sapiens	Human secreted protein encoded by 5' EST	414	76
549	688	Y73463	Homo sapiens	Human secreted protein clone	701	98

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				yk199_1 protein sequence		
550	6897	gi5815180	Homo sapiens	unknown	509	97
551	690	gi10645186	Homo sapiens	meningioma-expressed antigen 5s splice variant	522	100
552	6909	W78149	Homo sapiens	Human secreted protein encoded by gene 24 clone HSVBF78.	485	100
553	6924	Y35923	Homo sapiens	Extended human secreted protein sequence,	514	99
554	6937	G03798	Homo sapiens	Human secreted protein,	281	70
555	6951	gi511857	Homo sapiens	prostate-specific antigen	364	95
556	7008	G03200	Homo sapiens	Human secreted protein,	548	98
557	7009	Y22213	Homo sapiens	Human V201 protein sequence.	856	100
558	7057	gi6003654	Homo sapiens	brain specific membrane-anchored protein BSMAP	1814	100
559	7098	W27291	Homo sapiens	Human H1075-1 secreted protein 5' end.	712	100
560	7114	gi3212110	Homo sapiens	prefoldin subunit 1	534	98
561	712	gi4558641	Homo sapiens	P85B_HUMAN; PTDINS-3-KINASE P85-BETA	470	74
562	7215	gi4868366	Homo sapiens	delta-6 fatty acid desaturase	2437	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
563	7244	Y12445	Homo sapiens	Human 5' EST secreted protein	428	100
564	7248	gi311376	Homo sapiens	Humig	633	100
565	7252	gi5689531	Homo sapiens	KIAA1097 protein	5240	100
566	7292	gi5106998	Homo sapiens	HSPC040 protein	580	100
567	7306	Y32201	Homo sapiens	Human receptor molecule (REC) encoded by Incyte clone 2057886.	1974	95
568	7338	Y73880	Homo sapiens	Human prostate tumor EST fragment derived protein #67.	1566	100
569	736	gi10178317	Homo sapiens		1468	100
570	737	G00851	Homo sapiens	Human secreted protein,	522	98
571	740	W85610	Homo sapiens	Secreted protein clone eh80_1.	1115	87
572	7400	Y93948	Homo sapiens	Amino acid sequence of a lectin ss3939 polypeptide.	1982	98
573	7415	gi3043670	Homo sapiens	KIAA0573 protein	2392	100
574	7429	Y40864	Homo sapiens	A human glutathione-S-transferase (hGST) protein.	1183	99
575	7458	Y53643	Homo sapiens	A bone marrow secreted protein designated BMS6.	554	99
576	7516	gi4468311	Homo sapiens		1146	99
577	7526	gi4138922	Homo sapiens	promyelocytic leukemia zinc finger	3571	99

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				protein; kruppel-like zinc finger protein; PLZF		
578	7571	G02915	Homo sapiens	Human secreted protein,	209	100
579	7614	W74726	Homo sapiens	Human secreted protein fg949_3.	1879	100
580	7663	gi5912548	Homo sapiens		1634	100
581	7686	gi4929711	Homo sapiens	CGI-121 protein	870	100
582	7714	gi388765	Homo sapiens	phospholipase D	4428	99
583	7724	G03933	Homo sapiens	Human secreted protein,	570	100
584	7834	gi8919166	Homo sapiens	mesenchymal stem cell protein DSC92	1133	100
585	7855	Y48505	Homo sapiens	Human breast tumour-associated protein 50.	684	100
586	7870	Y13372	Homo sapiens	Amino acid sequence of protein PRO223.	2559	100
587	7871	Y91689	Homo sapiens	Human secreted protein sequence encoded by gene 93	768	100
588	7892	gi34659	Homo sapiens	macrophage inflammatory protein-2alpha precursor	532	100
589	7927	gi32575	Homo sapiens		183	91
590	7944	gi1657458	Sus scrofa	calcium/calmodulin-dependent protein kinase II isoform gamma-B	2744	100
591	7947	G01131	Homo sapiens	Human	574	96

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				secreted protein,		
592	800	gi3021428	Homo sapiens	neutral sphingomyelinase	167	68
593	8055	gi4929637	Homo sapiens	CGI-84 protein	1038	100
594	8082	gi4679014	Homo sapiens	HSPC014	715	100
595	8127	gi9955693	Homo sapiens	twisted gastrulation protein	905	95
596	8174	gi5532294	Homo sapiens	MUM2	767	100
597	8178	gi4530587	Homo sapiens	TADA1 protein	1132	100
598	8215	R66278	Homo sapiens	Therapeutic polypeptide from glioblastoma cell line.	830	100
599	8263	Y48371	Homo sapiens	Human prostate cancer-associated protein 68.	713	98
600	827	gi3172337	Cavia porcellus	phospholipase B	955	73
601	828	Y29517	Homo sapiens	Human lung tumour protein SAL-82 predicted amino acid sequence.	833	94
602	8294	gi4929767	Homo sapiens	CGI-149 protein	1085	100
603	8313	gi5771420	Homo sapiens	group IID secretory phospholipase A2	852	100
604	832	Y86260	Homo sapiens	Human secreted protein HELHN47,	319	78
605	8357	gi4191358	Mus musculus	claudin-7	164	47
606	8373	gi1945271	Homo sapiens	protein phosphatase 6	1666	100
607	8379	gi58529	Homo sapiens		1226	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		81		cardiotrophin-like cytokine CLC		
608	8380	gi3402216	Homo sapiens	protein	974	100
609	8386	gi3869888	Homo sapiens	oncostatin M	1297	99
610	8418	Y70210	Homo sapiens	Human TANGO 130 protein.	722	98
611	8442	G01895	Homo sapiens	Human secreted protein,	490	95
612	8457	G04048	Homo sapiens	Human secreted protein,	450	98
613	8458	W97119	Homo sapiens	S-adenosyl-L-methyltransferase (SAM-MT) protein.	1484	100
614	8469	gi7159799	Homo sapiens		255	100
615	8480	gi4589530	Homo sapiens	KIAA0943 protein	1998	100
616	8521	gi5726235	multiple sclerosis associated retrovirus element	unknown protein U5/2	250	82
617	857	gi9663958	Homo sapiens	cysteinyl leukotriene CysLT2 receptor	612	99
618	8574	gi6841260	Homo sapiens	HSPC305	1049	100
619	8606	gi3367707	Homo sapiens	scrapie responsive protein 1	544	100
620	8632	G01158	Homo sapiens	Human secreted protein,	502	100
621	8646	gi3882249	Homo sapiens	KIAA0764 protein	2175	100
622	8666	Y66196	Homo sapiens	Human bladder tumour EST encoded protein 54.	1080	95
623	8675	gi9963908	Homo sapiens	NPD009	432	96
624	8683	G04018	Homo sapiens	Human	469	98

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				secreted protein,		
625	8708	gi1633564	Homo sapiens	C8	364	98
626	8720	gi8248465	Homo sapiens	hepatocellular carcinoma-associated antigen 56A	191	69
627	8756	Y94984	Homo sapiens	Human secreted protein vel1_1,	369	97
628	8765	Y00346	Homo sapiens	Fragment of human secreted protein encoded by gene 2.	1068	97
629	8783	Y27918	Homo sapiens	Human secreted protein encoded by gene No. 123.	1051	95
630	8804	Y25426	Homo sapiens	Human SIGIRR protein.	887	100
631	8838	Y99409	Homo sapiens	Human PRO1343 (UNQ698) amino acid sequence	1279	100
632	8851	W74785	Homo sapiens	Human secreted protein encoded by gene 56 clone HSAXS65.	454	100
633	8853	W75116	Homo sapiens	Human secreted protein encoded by gene 60 clone HILCJ01.	245	95
634	8857	gi2565196	Homo sapiens	non-functional folate binding protein	479	74
635	8859	Y02690	Homo sapiens	Human secreted protein encoded by gene 41c lone	600	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				HSZAF47.		
636	8901	Y86491	Homo sapiens	Human gene 59-encoded protein fragment,	548	99
637	8907	W88745	Homo sapiens	Secreted protein encoded by gene 30 clone HTSEV09.	2004	99
638	8934	W75088	Homo sapiens	Human secreted protein encoded by gene 32 clone HAGBB70.	421	98
639	8960	Y02693	Homo sapiens	Human secreted protein encoded by gene 44 clone HTDAD22.	267	72
640	8979	Y76143	Homo sapiens	Human secreted protein encoded by gene 20.	1374	98
641	8980	Y11433	Homo sapiens	Human 5' EST secreted protein	466	100
642	8986	G02626	Homo sapiens	Human secreted protein,	306	100
643	8987	G02093	Homo sapiens	Human secreted protein,	486	97
644	8995	Y12908	Homo sapiens	Human 5' EST secreted protein	181	100
645	9035	Y71108	Homo sapiens	Human Hydrolase protein-6 (HYDRL-6).	800	100
646	9062	gi8886005	Homo sapiens	lysophosphatidic acid acyltransferase-delta	523	100
647	9074	Y25761	Homo sapiens	Human	1366	99

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				secreted protein encoded from gene 51.		
648	9075	Y73336	Homo sapiens	HTRM clone 1852290 protein sequence.	1591	100
649	9098	Y57878	Homo sapiens	Human transmembrane protein HTMPN-2.	516	100
650	9109	gi23903	Homo sapiens	63kDa protein kinase	1141	97
651	911	gi32456	Homo sapiens	protein-tyrosine phosphatase	2591	100
652	912	gi1136743	Homo sapiens	human P5	212	46
653	9163	Y34129	Homo sapiens	Human potassium channel K+Hnov28.	377	71
654	9164	Y41324	Homo sapiens	Human secreted protein encoded by gene 17 clone HNFIY77.	1083	99
655	9173	gi6851256	Mus musculus	protein tyrosine phosphatase-like protein PTPLB	631	93
656	9187	Y66721	Homo sapiens	Membrane-bound protein PRO511.	1173	95
657	9190	W40378	Homo sapiens	Human breast cancer protein CH14-2a16-1 from 2.0 kB DNA fragment #2.	792	81
658	9194	Y02781	Homo sapiens	Human secreted protein.	462	70
659	9210	G02994	Homo sapiens	Human secreted protein,	166	80

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
660	9222	G02520	Homo sapiens	Human secreted protein,	186	43
661	9230	gi6706554	Homo sapiens	inositol 1,4,5-trisphosphate 3-kinase B	1315	95
662	9258	gi522145	Homo sapiens	B-cell growth factor	120	56
663	9260	G04072	Homo sapiens	Human secreted protein,	138	51
664	9271	gi6690095	Homo sapiens	tetraspanin protein	317	67
665	9272	gi163042	Bos taurus	factor activating exoenzyme S	444	72
666	9275	gi401774	Homo sapiens	ribosomal protein S6 kinase 3	424	81
667	930	G02355	Homo sapiens	Human secreted protein,	167	41
668	9304	gi8979743	Canis familiaris	Band4.1-like5 protein	1493	93
669	9346	gi2738989	Mus musculus	high mobility group protein homolog HMG4	384	89
670	9347	gi36613	Homo sapiens	serine/threonine protein kinase	199	91
671	935	gi5541870	Homo sapiens	QA79 membrane protein, allelic variant airm-1b	334	57
672	9350	gi3327124	Homo sapiens	KIAA0655 protein	757	87
673	9351	W57260	Homo sapiens	Human semaphorin Y.	573	95
674	9356	gi59977	Human endogenous retrovirus	tripartite fusion transcript PLA2L	127	59
675	9363	Y17834	Homo sapiens	Human PRO361 protein sequence.	968	92
676	9366	gi72431	Homo sapiens	KIAA1374	649	96

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		29		protein		
677	9369	G03793	Homo sapiens	Human secreted protein,	222	69
678	9378	gi4468311	Homo sapiens		163	39
679	9393	gi2738989	Mus musculus	high mobility group protein homolog HMG4	384	89
680	9444	G01399	Homo sapiens	Human secreted protein,	157	93
681	9467	gi4454702	Homo sapiens	HSPC007	230	71
682	9486	gi10047243	Homo sapiens	KIAA1584 protein	605	93
683	949	Y30895	Homo sapiens	Human secreted protein fragment encoded from gene 25.	704	99
684	9499	W36002	Homo sapiens	Human Fchd531 gene product.	2173	96
685	9510	gi1665799	Homo sapiens		867	83
686	9523	Y53022	Homo sapiens	Human secreted protein clone qf116_2 protein sequence	1252	89
687	9534	Y66670	Homo sapiens	Membrane-bound protein PRO1180.	998	100
688	9539	Y76144	Homo sapiens	Human secreted protein encoded by gene 21.	633	100
689	954	G02490	Homo sapiens	Human secreted protein,	160	78
690	9546	gi181121	Homo sapiens	chorionic somatomammotropin	616	96
691	955	gi7243103	Homo sapiens	KIAA1361 protein	2042	100
692	9551	gi17723	Homo sapiens	ras-related	341	57

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		45		GTP-binding protein		
693	9558	W88403	Homo sapiens	Human adult testis secreted protein ga63_6.	2252	100
694	9561	gi6690017	Herpesvirus papio	NTR	100	30
695	957	Y86260	Homo sapiens	Human secreted protein HELHN47,	319	78
696	9572	gi972940	Mus musculus	Elf-1	806	92
697	9576	gi3249005	Homo sapiens	geminin	448	98
698	9586	gi2887288	Homo sapiens	mRNA cleavage factor I 25 kDa subunit	208	100
699	9587	G00995	Homo sapiens	Human secreted protein,	726	99
700	9592	gi495273	Rattus norvegicus	ribosomal protein S15a	202	78
701	9595	gi7799912	Homo sapiens	UBASH3A protein	453	47
702	9610	Y07875	Homo sapiens	Human secreted protein fragment encoded from gene 24.	574	100
703	9634	Y73325	Homo sapiens	HTRM clone 001106 protein sequence.	820	99
704	9639	G00805	Homo sapiens	Human secreted protein,	155	67
705	9647	G03786	Homo sapiens	Human secreted protein,	196	73
706	9653	gi3882341	Homo sapiens	KIAA0810 protein	523	100
707	9654	G01924	Homo sapiens	Human secreted protein,	469	100
708	9678	Y99376	Homo sapiens	Human PRO1244 (UNQ628) amino	474	100

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				acid sequence		
709	9709	Y11825	Homo sapiens	Human 5' EST secreted protein	657	100
710	9722	gi7677422	Mus musculus	GTPase Rab37	189	75
711	9731	Y12424	Homo sapiens	Human 5' EST secreted protein	207	100
712	9742	Y57954	Homo sapiens	Human transmembrane protein HTMPN-78.	484	100
713	9749	gi3687829	Homo sapiens	hT41	386	65
714	9755	gi2055295	Homo sapiens	Similar to a C.elegans protein in cosmid C14H10	2583	100
715	9762	G03436	Homo sapiens	Human secreted protein,	176	61
716	9763	gi6180011	Homo sapiens	anaphase-promoting complex subunit 4	1016	100
717	9784	G03570	Homo sapiens	Human secreted protein,	401	96
718	9794	G00803	Homo sapiens	Human secreted protein,	333	69
719	9795	gi2516242	Mus musculus	Rab33B	669	94
720	9798	gi558599	Homo sapiens	ZID, zinc finger protein with interaction domain	605	96
721	9805	Y25881	Homo sapiens	Human secreted protein fragment encoded from gene 61.	566	96
722	9816	gi532056	Homo sapiens	protein-tyrosine-phosphatase	384	100
723	9830	G00857	Homo sapiens	Human	539	96

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
				secreted protein,		
724	9836	G00914	Homo sapiens	Human secreted protein,	527	100
725	9837	gi2662099	Homo sapiens	KIAA0409	230	67
726	984	Y29517	Homo sapiens	Human lung tumour protein SAL-82 predicted amino acid sequence.	833	94
727	9849	gi7229305	Homo sapiens	ZNF264, partial cds	140	90
728	9851	gi5262560	Homo sapiens	hypothetical protein	369	64
729	9859	gi3881976	Homo sapiens	hypothetical protein	167	93
730	9863	gi7295707	Drosophila melanogaster	CG15433 gene product	837	78
731	9888	gi3319677	Homo sapiens		209	72
732	989	gi4557143	Rattus norvegicus	zinc finger protein RIN ZF	604	92
733	9919	G01843	Homo sapiens	Human secreted protein,	586	100
734	9922	W67869	Homo sapiens	Human secreted protein encoded by gene 63 clone HHGDB72.	551	93
735	9947	W78239	Homo sapiens	Fragment of human secreted protein encoded by gene 3.	251	78
736	9956	Y36203	Homo sapiens	Human secreted protein #75.	273	77
737	9961	Y99357	Homo sapiens	Human PRO1190 (UNQ604) amino acid sequence	650	99
738	9972	Y12149	Homo sapiens	Human 5' EST secreted protein	284	100
739	9977	gi10039	Homo sapiens	osteoblast	822	98

SEQ ID NO:	SEQ ID NO: in USSN 09/488,725	Accession No.	Species	Description	Smith-Waterman Score	% Identity
		439		differentiation promoting factor		

Table 3 - Amino Acids

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
1	740	2	557	FVGRLLRLGEALRLRPDPSGGCRLQPALVGETEMSEKENNFPP LPKFIPVKPCFYQNFSDEIPVEHQVLVKRIYRLWMFYCATLGV NLIACLAWWIGGGSGTNFGLAFVWLLLFTPCGYVCWFRPVYKA FRADSSFNFMAFFFIFRSPVCPDRHPGDWLLRLGRVRLAVGNW ILPVQPGRCRGHA
2	741	305	838	FLGAGADIFCAYLRMSSKQATSPFACAADGEDAMTQDLTSREK EEGSDQHVASHLPLHPIMHNKPHSEELPTLVSTIQQDADWDSV LSSQQRMESENNKLCSLYSFRNTSTSPHKPDEGSRDREIMTSV TFGTPERRKGSLADVVDTLKQKKLEEMTRTEQEDSSCMEKLLS KDWKE
3	742	12	1315	EGYLTGRPTRPVAVRGKSTADLRMMGRSPGFAMQHIVGVPHVL VRRGLLGRDLFMTRTLCSPGPSQPGEKRPEEVALGLHHRLPAL GRALGHSIQQRATSTAKTWWDRYEEFVGLNEVREAQGKVTEAE KVFMVARGLVREAREDLEVHQAKLKEVRDRLDRVSREDSQYLE LATLEHRMLQEEKRLRTAYLRAEDSEREKFSLFSAAVRESHEK ERTRAERTKNWSLIGSVLGALIGVAGSTYVNRVRLQELKALLL EAQKGPVSLQEAIREQASSYSRQQRDLHNLMVDLRGLVHAAGP GQDSGSQAGSPPTRDRDVDVLSAALKEQLSHSRQVHSCLEGLR EQLDGLEKTCSQMAGVVQLVKSAAHPGLVEPADGAMPSFLLEQ GSMILALSDTEQRLEAQVNRNTIYSTLVTCVTFVATLPVLYML FKAS
4	743	112	745	NLPPLTPQPGPRLAGSGPSHWFSPLSLPVASKAPGTMAQALGE DLVQPPELQDDSSSLGSDSELSGPGPYRQADRYGFIGGSSAEP GPGHPPADLIRQREMKWVEMTSHWEKTMSRRYKKVKMQCRKGI PSALRARCWPLLCGAHVCQKNSPGTYQELAEAPGDPQWMETIG RDLHRQFPLHEMFVSPQGHGQQGLLQVLKAYTLYRPEQG
5	744	99	265	LRGMAAAAAGPAASQRFFQSFSDALIDQDPQAALEVGEPFLLP PLPADPPPSSTA

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
6	745	210	758	WACFRSAHCSRHLRNRIFMYLYWDKTRSPVCKGPALREERPQP RLKLEDYKDRLKSGEHLNPDQLEAVEKYEEVLHNLEFAKELQK TFSGLSLDLLKAQKKAQRREHMLKLEAEKKKLRTILQVQYVLQ NLTQEHVQKDFKGGLNGAVYLPSKELDYLIKPSKLTCPERNES LRQTLEGSTV
7	746	48	450	XAGVQMKLEFLQRKFWAATRQCSTVDGPCTQSCEDSDLDCFVI DNNGFILISKRSRETGRFLGEVDGAVLTQLLSMGVFSQVTMYD YQAMCKPSSHHHSAAQPLVSPISAFLTATRWLLQELVLFLLEW SVWGSX*
8	747	1	469	CRGRLAQLEEAAVAATMSAGDAVCTGWLVKSPPERKLQRYAWR KRWFVLRRGRMSGNPDVLEYYRNKHSSKPIRVIDLSECAVWKH VGPSFVRKEFQNNFVFIVKTTSRTFYLVAKTEQEMQVWVHSIS QVCNLGHLEDGAADSMESLSYTRSYLQ
9	748	242	409	IPAVPLTSCVTVGSYSLSVRDYDPRQGDTVKHYKIRTL\DKRG FYISP\RSTFSTLQ
10	749	1	1146	KDSVLNIARGKKYGEKTKRVSSRKKPALKC/TSQKQPALKAIC DKEDSVPNTATEKKDEQISGTVSSQKQPALKATSDKKDSVSNI PTEIKDGQQSGTVSSQKQPAWKATSVKKDSVSNIATEIKDGQI \RGTVSSQRQPALKA\TGDEKDSVSNIAREIKDGEKSGTVSPQ KQSAQKVIFKKKVSLLNIATRITGGWKSGTEYPENLPTLKATI ENKNSVLNTATKMKDVQTSTPEQDLEMASEGEQKRLEEYENNQ PQVKNQIHSRDDLDDIIQSSQTVSEDGDSLCCNCKNVILLIDQ HEMKCKDCVHLLKIKKTFCLCKRLTELKDNHCEQLRVKIRKLK NKASVLQKRLSEKEEIKSQLKHETLELEKELCSLRFAIQQ
11	750	3	892	SPLRYRAGQSGSTISSSSCAMWRCGGRQGLCVLRRLSGGHAHH RAWRWNSNRACERALQYKLGDKIHGFTVNQVTSVPELFLTAVK LTHDDTGARYLHLAREDTNNLFSVQFRTTPMDSTGVPHILEHT VLCGSQKYPCRDPFFKMLNRSLSTFMNAFTASDYTLYPFSTQN PKDFQNLLSVYLDATFFPCLRELDFWQEGWRLEHENPSDPQTP LVFKGVVFNEMKGAFTDNERIFSQHLQNRLLPDHTYSVVSGGD PLCIPELTWEQLKQFHATHYHPSNARFFTYGNFPLDQH
12	751	367	856	RGAKAKSAVLPPGPPCSSILILSPPAPLTPRSPGTEATRPTAM SKSLKKKSHWTSKVHESVIGRNPEGQLGFELKGGAENGQFPYL GEVKPGKVAYESGSKLVSEELLLEVNETPVAGLTIRDVLAVIK HCKDPLRLKCVKQGESSGLLSVLPGGGTARGAGQ
13	752	144	442	SHRPQPDAWRQGNAFQCVQKEKMQVSSAEVRIGPMRLTQDPIQ VLLIFAKEDSQSDGFWWACDRAGYRCNIARTPESALECFLDKH HEIIVIDHRQTQN
14	753	1	581	FRLAGCGHLLVSLLGLLLLLARSGTRALVCLPCDESKCEEPRN CPGSIVQGVCGCCYTCASQRNESCGGTFGIYGTCDRGLRCVIR PPLNGDSLTEYEAGVCEDENWTDDQLLGFKPCNENLIAGCNII NGKCECNTIRTCSNPFEFPSQDMCLSALKRIEEEKPDCSKARC EVQFSPRCPEDSVLIEGYAPP

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
15	754	1	219	FRMAANVGSMFQYWKRFDLQQLQRELDATATVLANRQDESEQS RKRLIEQSREFKKNTPEVRRVTIVFALKGS
16	755	313	562	ETLSCRIMDHPSREKDERQRTTKPMAQRSAHCSRPSGSSSSSG VLMVGPNFRVGKKIGCGNFGELRLGEGLPQVYYFGPCGKY
17	756	273	574	GCCKD*HSGVIGRSWAMLFASGGFQVKLYDIEQQQIRNALENI RWASRRSPEGMEVGLFLSVGLVCHILKAMRICDVTFSSDGYCS ASELVKARPTVAGM
18	757	3	390	NSRVDDFVSARPKPRPLPRARGMVVVTGREPDSRRQDGAMSSS DAEDDFLEPATPTATQAGHAL/PPAAT/GSFLRLFPLTSEGLT SLHACPHCGATKTPCWQPCSVGGTTSPRTPRAGTSSTEMAHTL EMC
19	758	98	461	RALWVGGCSGEACGIGMSGLLTDPEQRAQEPRYPGFVLGLDVG SSVIRCHVYDRAARVCGSSVQKVENLYPQIGWVEIDPDVLWIQ FVAVIKEAVKAAGIQMNQIVGLGISTQRATFITWN
20	759	100	731	GLAAEQSMQFVKLWCGCSGEFPTRLRRRTPLTEAMEGGPAVCC QDPRAELVERVAAIDVTHLEEADGGPEPTRNGVDPPPRARAAS VIPGSTSRLLPARPSLSARKLSLQERPAGSYLEAQAGPYATGP ASHISPRAWRRPTIESHHVAISDAEDCVQLNQYKLQSEIGKGA YGVVRLAYNESEDRHYAMKVLSKKKLLKQYGFPRRPPP
21	760	2	520	FVYGKPVTLWPTISSVVPSTFLGLGNYEVEVEAEPDVRGPEIV TMGENDPPAVEAPFSFRSLFGLDDLKISPVAPDADAVAAQILS LLPLKFFPIIVIGIIALILALAIGLGIHFDCSGKYRCRSSFKC IELIARCDGVSDCKDGEDEYRCVRVGGQNAALQVFTAASRKTM
22	761	158	470	SLAMPFGCVTLGDKKNYNQPSEVTDRYDLGQVIKTEEFCEIFR AKDKTTGKLHTCKKFQKRDGRKVRKAAKNEIGILKMVKHPNIL QLVDVFVTRKEYFIFLEL
23	762	1	749	QRRRFRAGLWGGHGLTDGLRRNGGCGCSARVPRVGERLRGHRC PDPLCLLLDMLFLSFHAGSWESWCCCCLIPADRPWDRGQHWQL EMADTRSVHETRFEAAVKVIQSLPKNGSFQPTNEMMLKFYSFY KQATEGPCKLSRPGFWDPIGRYKWDAWSSLGDMTKEEAMIAYV EEMKKIIETMPMTEKVEELLRVIGPFYEIVEDKKSGRSSDITS DLGNVLTSTPNAKTVNGKAESSDSGAESEEEEAC
24	763	3	558	SCFKGRTGGRSGSSGDSSRWARCGRHFSASTEEPPLSQPCSAL PRSGRRGCAVPSSVTKMLSFFRRTLGRRSMRKHAEKERLREAQ RAATHIPAAGDSKSIITCRVSLLDGTDVSVDLPKKAKGQELFD QIMYHLDLIESDYFGLRFMDSAQVAHWLDGTKSIKKQVKIGSP YCLHLRVKFYSS
25	764	9	424	ESRERSGNRRGAEDRGTCGLQSPSAMLGAKPHWLPGPLHSPGL PLVLVLLALGAGWAQEGSEPVLLEGECLVVCEPGRAAAGGPGG AALGEAPPGRVAFAAVRSHHHEPAGETGNGTSGAIYFDQVLVN EGGGFDRAS

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26	765	2	507	EDVKSYYTVHLPQLENINSGETRTISHFHYTTWPDFGVPQSPA SFLNFLFKVRESGSLNPDHGPVVIHRSAGTGRSSTFSVVHTCL VLMEKGDDINIKQVLLNIRKFQMGLI\QTPDQLRFSYMAITEG AKCVKGDSSIQKRWKELSKE/DLPPAFDHSPNKIMTEKYNR
27	766	84	852	LNRQRCGDQVLVPGTGLAAILRTLPMFHDEEHARARGLSEDTL VLPPASRNQRILYTVLECQPLFDSSDMTIAEWVCLAQTIKRHY EQYHGFVVIHGTDTMAFAASMLSFMLENLQKTVILTGAQVPIH ALWSDGRENLLGALLMAGQYVIPEVCLFFQNQLFRGNRATKVD ARRFAAFCSPNLLPLATVGADITINRELVRKVDGKAGLVVHSS MEQDVGLLRLYPGIPAALVRAFLQPPLKGVVMETFGSGNG
28	767	992	210	LFRLAPGFLRSLARQGYHQIWAFPFLPSGATATWPAASRSRSL AARSLPRSPARPGPNDALLGEHDFRGQGVRAQRFRFSEEPGPG ADGAVLEVHVPQIGAGVSLPGILAAKCGAEVILSDSSELPHCL EVCRQSCQMNNLPHLQVVGLTWGHISWDLLALPPQDIILASDV FFEPEDFEDILATIYFLMHKNPKVQLWSTYQVRSADWSLEALL YKWDMKCVHIPLESFDADKEDIAESTLPGRHTVEMLVISFAKD SL
29	768	23	624	SFIYKHTHRARFGPRAIVASPALTAGPHVSLTASCRVGMWVSC SPSPFLHPTNTLVAVLERDTLGIREVRLFNAVVRWSEAECQRQ QLQVTPENRRKVLGKALGLIRFPLMTIEEFAAGNRARAQGLVW EGSGTQVGIW/CTEDSAPEFTAESLADAWHIQIGRNLACEDAS T/WAIC*PRPGSVPTVHTARPRLSCLSSCF
30	769	100	2	MASTQDAELAVSRXRAIALXPGXQSXXPSQKKK
31	770	158	1957	LLKSCGVLLSGVCIPCEGKGPTVLVIQTAVPQDRPTKSSMRSA AKPWNPAIRAGGHGPDRVRPLPAASSGMKSSKSSTSLAFESRL SRLKRASSEDTLNKPGSTAASGVVRLKKTATAGAISELTESRL RSGTGAFTTTKRTGIPAPREFSVTVSRERSVPRGPSNPRKSVS SPTSSNTPTPTKHLRTPSTKPKQENEGGEK\VRLSPK/FRELL AEAKAKDSEINRLRSELKKYKEKRTLNAEGTDALGPNVDGTSV SPGDTEPMIRALEEKNKNFQKELSDLEEENRVLKEKLIYLEHS PNSEGAASHTGDSSCPTSITQESSFGSPTGNQLSSDIDEYKKN IHGNALRTSGSSSSDVTKASLSPDASDFEHITAETPSRPLSST SNPFKSSKCSTAGSSPNSVSELSLASLTEKIQKMEENHHSTAE ELQATLQELSDQQQMVQELTAENEKLVDEKTILETSFHQHRER AEQLSQENEKLMNLLQERVKNEEPTTQEGKIIELEQKCTGILE QGRFEREKLLNIQQQLTCSLRKVEEENQGALEMIKRLKEENEK LNEFLELERHNNNMMAKTLEECRVTLEGLKMENGSLKSHLQG
32	771	203	514	SQMHRLIFVYTLICANFCSCRDTSATPQSASIKALRNANLRRD ESNHLTDLYRRDETIQVKGNGYVQSPRFPNSYPRNLLLTWRLH SQENTRIQLVFDNQFGL

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33	772	59	713	PFKKMTDLLRSVVTVIDVFYKYTKQDGECGTLSKGELKELLEK ELHPVLKNPDDPDTVDVIMHMLDRDHDRRLDFTEFLLMIFKLT MACNKVLSKEYCKASGSKKHRRGHRHQEEESETEEDEEDTPGH KSGYRHSSWSEGEEHGYSSGHSRGTVKCRHGSNSRRLGRQGNL SSSGNQEGSQKRYHRSSCGHSWSGGKDRHGSSSVELRERINKS HIK
34	773	209	601	VPKISGPDHIDFIPWDQLFMASSSSVTEFLVLGFSSLGELQLV LFAVFLCLYLIILSGNIIIISVIHLDHSLHTPMYFFLGILSIS EIFYTTVILPKMLINLFSVFRTLSFVSCATQMFYEIVGPGTQE R
35	774	373	987	DHSTETPGIPAAEPVSHGTGKLERAPTLPAGAELPAPAAVPCP TL*VC/LYPQLLGLSVATMVTLTYFGAHFAVIRRASLEKNPYQ AVHQWGTQQRLIQHPESGSEGQSLLGPLRAFSAGLSLVGLLTL GAVLSAAATVREAQGLMAGGFLCFSLAFCAQVQVVFWRLHSPT QVEDAMLDTYDLVYEQAMKGTSHVRRQELAAIQ
36	775	102	466	QPGYSEYDKNRGQGMLLNMMCGRQLSAISLCLAVTFAPLFNAQ ADEPEVIPGDSPVAVSEQGEALPQAQATAIMAGIQPLPEGAAE KARTQIESQLPAGYKPVYLNQLQLLYAARGISCSV
37	776	2	430	RTRAADVYVFSLTGKSRNVSSSTVRRSAVGGMSALALFDLLKP NYALATQVEFTDPEIVAEYITYPSPNGHGEVRGYLVKPAKMSG KTPAVVVVHENRGLNPYIEDVARRVAKAGYIALAPDGLSSVGG YPGNDIKVVSAAA
38	777	106	556	VKQRHGNSLLTTETKCISCRLGVPLSPQRRFQAIRIEEVKLRW FAFLIVLLAGCSSKHDYTNPPWNAKVPVQRAMQWMPISQKAGA AWGVDPQLITAIIAIESGGNPNAVSKSNAIGLMQLKASTSGRD VYRRMGWSGEPTTSELKNSSR
39	778	3	892	HAAGIRHEAKPKRSFYAARDLYKYRHQYPNFKDIRYQNDLSNL RFYKNKIPFKPDGVYIEEVLSKWKGDYEKLEHNHTYIQWLFPL REQGLNFYAKELTTYEIEEFKKTKEAIRRFLLAYKMMLEFFGI KLTDKTGNVARAVNWQERFQHLNESQHNYLRITRILKSLGELG YESFKSPLVKFILHEALVENTIPNIKQSALEYFVYTIRDRRER RKLLRFAQKHYTPSENFIWGPPRKEQSEGSKAQKMSSPLASSH NSQTSMHKKAKDSKNSSSAVHLNSKTAEDKKVAPKEPV
40	779	123	395	ELQVFQPIGGMSDSGSQLGSMGSLTMKSQLQITVISAKLKENK KNWFGPSPYVEVTVDGQSKKTEKCNNTNSPKWKQPLTVIVTPV SKLH
41	780	173	438	IETLSFVIRNWNTHAMSKPIVMERGVKYRDADKMALIPVKNVA TEREALLRKPEWMKIKLPADSTRIQGIKAAMRKNGLHSVCEEA SC
42	781	287	393	PRMVLGKPQTDPTLEWFLSHCHIHKYPSKSTLIPQ
43	782	119	556	GLRISVQERIKACFTESIQTQIAAAEALPDAISRAAMTLVQSL LNGNKILCCGNGTSAANAQHFAASMINRFETERPSLPAIALNT DNVVLTAIANDRLHDEVYAKQVRALGHAGDVLLAISTRGNSRD IVKAVEAAVTRDTTIV

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44	783	248	554	KQTQHAPGMMKKYLALALIAPLLISCSTTKKGDTYNEAWVKDT NGFDILMGQFAHNIENIWGFKEVVIAGPKDYVKYTDQYQTRSH INFDDGTITIEPIPGT
45	784	77	311	TDRTALNPGQESAMNRLFSGRSDMPFALLLLAPSLLLLGGLVA WPMVSNIEISFLRLPLNPNIESTFVGVSNYVRILS
46	785	184	627	KELVDEKSERGRAMDPVSQLASAGTFRVLKEPLAFLRALELLF AIFAFATCGGYSGGLRLSVDCVNKTESNLSIDIAFAYPFRLHQ VTFEVPTCEGKERQKLALIGDSSSSAEFFVTVAVFAFLYSLAA TGRYIFFHNKNRENNRGPL
47	786	3	742	LGTVSYGADTMDEIQSHVRDSYSQMQSQAGGNNTGSTPLRKAQ SSAPKVRKSVSSRIHEAVKAIVLCHNVTPVYESRAGVTEETEF AEADQDFSDENRTYQASSPDEVALVQWTESVGLTLVSRDLTSM QLKTPSGQVLSFCILQLFPFTSESKRMGVIVRDESTAEITFYM KGADVAMSPIVQYNDWLEEECGNMAREGLRTLVVAKKALTEEQ YQDFEVSRLPGIPSSYDGAFLTLKLVLPVFV
48	787	864	335	EGPHR\RLFQMVKA/LQEAPEDPNQILIGYSRGLVVIWDLQGS RVLYHFLSSQQLENIWWQRDGRLLVSCHSDGSYCQW\PVSSEA QQPEPLRSLVPYGPFPCKAITRILWLTTRQGLPFTIFQGGMPR ASYGDRHCISVIHDGQQTAFDFTSRVIGFTVLTEADPAASRRA SGVGAQG
49	788	410	951	KQGLEVRDLHFKEITSGRALLRVACKRPSMVPGGQLQRAGAGA QARITGLSPALWGARVHGWIPELPAGLPPGACLWPLIPACPSR HWGWVSAPVKG/WAQAILGLALCL/RGEHRGLGAGVSKVRSLK MDRKVWTETLIEVGMPLLATDTWGLPHSTAVWVSQPPPYLSDH STLELERDPL
50	789	1	437	LSCNSEQALLSLVPVQRELLRRRYQSSPAKPDSSFYKGLGTCP SQLRLSEPPPTPRHLSVASVSHHMFPSHRSLCPHLPDFFAAPF PSDNLPYTLQSPFPSPPPATPSDHALILHH\DLNGGPDDPLQQ TGQLFGGLVRDIRRRYP
51	790	1	198	SPSSKLVGMWWAGRAGSSRTTSVSLLCLP/SAPFGASNLLVNP LEPQNADKIKIKIADLGNACWVV
52	791	3	435	RVDPRVRAPRCGDKIKNHMY\KCDCGSLKDCASDRCCETSCTL SLGSVCNTGLCCHKCKYAAPGVVCRDLGGICDLPEYCDGKKEE CPNDIYIQDGTPCSAVSVCIRGNCSDRDMQCQALFGYQVKDGS PACYRKLNRIGNRFGT
53	792	1	728	PGRPTRPDASLAQ/DPRTTMFRIPEFKWSPMHQRLLTDLLFAL ETDVHVWRS\HSTKSVMDFVNSNENIIFVHNTIHLISQMVDNI IIACGGILPLLSAATSPTGSKTELENIEVTQGMSAETAVTFLS RLMAMVDVLVFASSLNFSEIEAEKNMSSGGLMRQCLKLVCCVA VRNCLECRQRQRDRGNKSSHGSSKPQEVPQSVTATAASKTPLE NVPGNLSPIKDPDRLLQDVDINRLRAVVF

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54	793	2230	990	NSSGVKLLQALGLSPGNGKDHSILHSRNDLEEAFIHFMGKGAA AERFFSDKETFHDIAQVASEFPGAQHYVGGNAALIGQKFAANS DLKVLLCGPVGPKLHELLDDNVFVPPESLQEVDEFHLILEYQA GEEWGQLKAPHANRFIFSHDLSNGAMNMLEVFVSSLEEFQPDL GGLSGLHMMEGQSKELQRKRLLEVVTSISDIPTGIPV\HLELG \SMTNRELMSSIV\LQQVFPAVTSLGLNEQELLFLTQSASGPH SSLSSWNGVPDVGMVSDILFWILKEHGRSKSRASDLTRIHFHT LVYHILATVDGHWANQLAAVAAGARVAGTQACATETIDTSRVS LRAPQEFMTSHSEAGSRIVLNPNKPVVEWHREGISFHFTPVLV CKDPIRTVGLGDAISAEGLFYSEVHPHY
55	794	249	3	DDSSGWGLEQLVVRWSLALWPRLECSGMISAHCNLCL/LGSSD SPASAPRVAGITDVCHHAWLVFVFLVVMGFPHVGHVGLELL
56	795	2	1176	LGEVLKCQQGVSSLAFALAFLQRMDMKPLVVLGLPAPTAPSGC LSFWEAKAQLAKSCKVLVDALRHNAAAAVPFFGGGSVLRAAEP APHASYGGIVSVETDLLQWCLESGSIPILCPIGETAARRSVLL DSLEVTASLAKALRPTKIIFLNNTGGLRDSSHKVLSNVNLPAD LDLVCNAEWVSTKERQQMRLIVDVLSRLPHHSSAVITAASTLL TELFSNKGSGTLFKNAERMLRVRSLDKLDQGRLVDLVNASFGK KLRDDYLASLRPRLHSIYVSEGYNAAAILTMEPVLGGTPYLDK FVVSSSRQGQGSGQMLWECLRRDLQTLFWRSRVTNPINPWYFK HSDGSFSNKQWIFFWFGLADIRDSYELVNHAKGLPDSFHKPAS DPGS
57	796	755	374	YHAPALQPGQQSKTLSQEKKNFFRPGAVAHTCNPSTLGGRGGR ITRSGDRDHPG*HGETPSLLKIQKKLAGRDGGRL*SQLLGRLR QENGVNPGGGGCSEPRLRHCTPAW*QSETISRKKRKKERKY
58	797	2	476	FRPIGIIRQALCSADGHQRRILTLRLGLLVIPFLPASNLFFRV GFVVPSVGCCVMLLFGFG/ALRKHTEKKKLIAAVVLGILLS/N DAERLRCAVRGGEWRSE/EAVFRGAVSVCPLSAEVRCNIGRNL AAKGNQTGAIRYHREAVSLNPKTKSSTREFRPC
59	798	3	711	KIADFGFSNLFTPGQLLKTWCGSPPYAAPELFEGKEYDGPKVD IWSLGVVLYVLVCGALPFDGSTLQNLRARVLSGKFRIPFFMST ECEHLIRHMLVLDPNKRLSMEQICKHKWMKLGDADPNFDRLIA ECQQLKEERQVDPLNEDVLLAMEDMGLDKEQTLQSLRSDAYDH YSAIYSLLCDRHKRHKTLRLGALPSMPRALGLSSTSQYP\AEQ AGTAMNISVPQVQLINPENQIV
60	799	2	344	AREFLGHRASITWS*ARVHHRFPKAEVA*P/SLLRTDLTEDRT KCCHGDLLECADDRADLVEDIWENQDSISTILIECCEKPLLEK SHCIAEVENDEMPADLPSLAADFVESKDV

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61	800	142	594	VPPKMKRGTSLHSRRGKPEAPKGSPQINRKSGQEMTAVMQSGR PRSSSTTDAPTGSAMMEIACAAAAAAAAACLPGEEGTAERIERL EVSSLAQTSSAVASSTDGSIHTDSVDGTPDPQRTKAAIAHLQQ KILKLTEQIKIAQTARRNRRPGS*KDCTP*KCLRKSDEALNRV LQQI\RVPPKMKRGTSLHSRRGKPEAPKGSPQINRKSGQEMTA VMQSGRPRSSSTTDAPTGSAMMEIACAAAAAAAACLPGEEGTA ERIERLEVSSLAQTSSAVASSTDGSIHTDSVDGTPDPQRTKAA IAHLQQKILKLTEQIKIAQTARRNRRPG
62	801	232	1299	MQTIERLVKERDDLMSALVSVRSSLADTQQREASAYEQVKQVL QISEEANFEKTKALIQCDQLRKELERQAERLEKELASQQEKRA IEKDMMKKEITKEREYMGSKMLILSQNIAQLEAQVEKVTKEKI SAINQLEEIQSQLASREMDVTKVCGEMRYQLNKTNMEKDEAEK EHREFRAKTNRDLEIKDQEIEKLRIELDESKQHLEQEQQKAAL AREECLRLTELLGESEHQLHLTRQEKDSIQQSFSKEAKAQALQ AQQREQELTQKIQQMEAQHDKTENEQYLLLTSQNTFLTKLKEE CCTLAKKLEQISQKTRSEIAQLSQEKRYTYDKLGKLQRRNEEL EEQCVQHGRST*
63	802	3	334	SYPVWWNSPLTAEVPPELLAAAGFFHTGHQDKVRCFFCYGGLQ SWKRGDDPWTEHAKWFPSCQFLLRSKGRDFVHSVQETHSQLLG SWDPWEEPEDAAPVAPSVPASGYPELPTPRREVQSESAQEPGG VSPAEAQRAWWVLEPPGARDVEAQLRRLQEERTCKVCLDRAVS IVFVPCGHLVC\AECAPGLQLCPI\CRSPCGPLRPCLWVP
64	803	70	456	MCSYREKKAEPQELLQLDGYTVDYTDPQPGLEGGRAFFNAVKE GDTVIFASDDEQDRILWVQAMYRATGQSHKPVPPTQVQKLNAK GGNVPQLDAPISQFYADRAQKHGMDEFISSNPCNFDHASLFEM *
65	804	2	1376	KQLIVLGNKVDLLPQDAPGYRQRLRERLWEDCARAGLLLAPGH QGPQRPVKDEPQDGENPNPPNWSRTVVRDVRLISAKTGYGVEE LISALQRSWRYRGDVYLVGATNAGKSTLFNTLLESDYCTAKGS EAIDRATISPWPGTTLNLLKFPICNPTPYRMFKRHQRLKKDST QAEEDLSEQEQNQLNVLKKHGYVVGRVGRTFLYSEEQKDNIPF EFDADSLAFDMENDPVMGTHKSTKQVELTAQDVKDAHWFYDTP GITKENCILNLLTEKEVNIVLPTQSIVPRTFVLKPGMVLFLGA IGRIDFLQGNQSAWFTVVASNILPVHITSLDRADALYQKHAGH TLLQIPMGGKERMAGFPPLVAEDIMLKEGLGASEAVADIKFSS AGWVSVTPNFKDRLHLRGYTPEGTVLTVRPPLLPYIVNIKGQR IKKSVAYKTKKPPSLMYNVRKKKGKINV
66	805	1	874	STVASMMHRQETVECLRKFNARRKLKGAILTTMLVSRNFSAAK SLLNKKSDGGVKPQSNNKNSLVSPAQEPAPLQTAMEPQTTVVH NATDGIKGSTESCNTTTEDEDLKAAPLRTGNGSSVPEGRSSRD RTAPSAGMQPQPSLCSSAMRKQEIIKITEQLIEAINNGDFEAY TKICDPGLTSFEPEALGNLVEGMDFHKFYFENLLSKNSKPIHT TILNPHVHVIGEDAACIAYIRLTQYIDGQGRPSNPAKSEE\TR VWH\RR\DGKWLNVHYHCSGAPCPHRCSELSHRGF

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67	806	3	1714	LPKNVVFVLDSSASMVGTKLRQTKDALFTILHDLRPQDRFSII GFSNRIKVWKDHLISVTPDSIRDGKVYIHHMSPTGGTDINGAL QRAIRLLNKYVAHSGIGDRRVSLIVFLTDGKPTVGETHTLKIL NNTREAARGQVCIFTIGIGNDVDFRLLEKLSLENCGLTRRVHE EEDAGSQLIGFYDEIRTPLLSDIRIDYPPSSVVQATKTLFPNY FNGSEIIIAGKLVDRKLDHLHVEVTASNSKKFIILKTDVPVRP QKAGKDVTGSPRPGGDGEGDTNHIERLWSYLTTKELLSSWLQS DDEPEKERLRQRAQALAVSYRFLTPFTSMKLRGPVPRMDGLEE AHGMSAAMGPEPVVQSVRGAGTQPGPLLKKPYQPRIKISKTSV DGDPHFVVDFPLSRLTVCFNIDGQPGDILRLVSDHRDSGVTVN GELIGAPAPPNGHKKQRTYLRTITILINKPERSYLEITPSRVI LDGGDRLVLPCNQSVVVGSWGLEVSVSANANVTVTIQGSIAFV ILIHLYKKPAPFQRHHLGFYIANSEGLSSNCRVFCESGILIQE LTQQSVAVAGR
68	807	2	841	FFLEQVSQYTFAMCSYREKKSEPQELMQLEGYTVDYTDPHPGL QGGCMFFNAVKEGDTVIFASDDEQDRILWVQAMYRATGQSYKP VPAIQTQKLNPKGGTLHADAQLYADRFQKHGMDEFISANPCKL DHAFLFRILQRQTLDHRLNDSYSCLGWFSPGQVFVLDEYCARY GVRGCHRHLCYLAELMEHSENGAVIDPTLLHYSFAFCAS\HVH GNRPDGIGTVSVEEKERFEEIKERLSSLLENQISHFRYCFPFG RPEGALKATLSLLERVLMKDIA
69	808	2	757	DGLLHEVLNGLLDRPDWEEAVKMPVGILPCGSGNALAGAVNQH GGFEPALGLDLLLNCSLLLCRGGGHPLDLLSVTLASGSRCFSF LSVAWGFVSDVDIQSERFRALGSARFTLGTVLGLATLHTYRGR LSYLPATVEPASPTPAHSLPRAKSELTLTPDPAPPMAHSPLHR SVSDLPLPLPQPALASPGSPEPLPILSLNGGGPELAGDWGGAG DAPLSPDPQLSSPPGSPKAALHSPV*KKAPVIPPDM
70	809	3	530	KGVPTLLMAAGSFYDILAITGFNTCLGIAFSTGSTVFNVLRGV LEVVIGVATGSVLGFFIQYFPSRDQDKLVCKRTFLVLGLSVLA VFSSVHFGFPGSGGLCTLVMAFLAGMGWTSEKAEVEKIIAVAW DIFQPLLFGLIG\AEVSI\SSLRPETVGLCVATVGI\AVLIRI FDYIF
71	810	228	541	LLKEVVVQASPVCKTCCSQLVRTPVTFTEVQNV/CRCSAGYLI SVCSYTSSDHNQCYAGTASLALLWIGGILKGCLLWKQFRWTER SHWNFGYWALWSPGNGNGC
72	811	173	404	ICTSTYLQIFPGKPSCFMCKGRLMCIYFILWYLGHYTSLHWNW CRYISDPNVD/ACPDPRNAEVSMTHTVPALMELID
73	812	2	586	LESLPGFKEIVSRGVKVDYLTPDFPSLSYPNYYTLMTGRHCEV HQMIGNYMWDPTTNKSFDIGVNKDSLMPLWWNGSEPLWVTLTK AKRKVYMYYWPGCEVEILGVRPTYCLEYKNVPTDINFANAVSD ALDSFKSGRADLAAIYHERIDVEGHHYGPASPQRKDALKA\VD TVLKYMTKWIQERGLQDRLNVII

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74	813	2	348	ARDFHPKQTLDFLRSDMANSKITEEVKRSIAQQYLDLTVA/LE QVDPDAEVDAAPSTTSSCGH*DSHAGS*RVLSLLGD*GPA*TG ANSMAGKLLLVAWLGFPDPFWGKELSDPAFK
75	814	2	366	KQSGDVTCNCTDGRLAPSCLTCVGHCIFGGYCTMNSKMMPECQ SPPHMTGPRCEEHVFSQHQPGHITSILIPML*LLLLVLVAGVI FCHKRRVQGAKGFQHQRMTNGAMNAQIANPTYKMY
76	815	420	681	TVENAGRWL*EEAEIQAELERLERVRNLHIRELKRINNEDNSQ FKDHPTLNERYLLLHLLGRGGFSEVYKVMYGLFWFFYTNVARI
77	816	37	428	MCEEFLVMGKGCSCVF*ILLSNPQMWWLNDSNPETDNRQESPS QENIDRVSD/MAFVPSAWTASGGVAWGNLGESGSRTGGVRAET LAPRLQV*PAHLRGHPRSNRGQGRPPWKAGKLGKCQEVLFRFA AF
78	817	1	358	FRAMFLAVQHDCRPMDKSAGSGHKSEEKREKMKRTLLKDWKTR LSYFLQNSSTPGKPKTGKKSKQQAFIK*VENPELANINS*LLN *KGEL**A*ANIQNLSCRPSPEEAQLWSEAFDE
79	818	1	169	GFFNFSSPKLKGWKINSSLVLEIRKNILRFLDAERDVSVVKSS FPSKDARHSSVHR*FTQLHWGPPSHTPARP*RGFFNFSSPKLK GWKINSSLVLEIRKNILRFLDAERDVSVVKSSFPSKDARHSSV HR
80	819	55	310	RIDDQQELKRVT*YSQKEYTKKKLHKKCNIIQADIKPDNILDN ESITILKLSDFGSASHVADNDITPSSSQTTSAASSPPRTLRR
81	820	1	134	SSKPWD*SLAPKHSG*TKNMDCYCIIPTCIGRERCYGTCIGDT V
82	821	187	360	NSSKKLVMEHQWKKYLRRNYQRMLNRLITLIGSCGVL*LISTI PTSRLKFLKETGHGTPMEEIPEEELSEDVEQIDHADRELRRGQ NLRCKGIHRLPTHIQVGQN
83	822	208	723	KWMLLHSFKIFCLSLYPQL*CPFEFFSHSATIFHELVYKQTKI ISSNQELIYEGRRLVLEPGRLAQHFPKTTEENPIFVVSREPLN TIGLIYEKISLPKVHPRYDLDGDASMAKAITGVVCYACRIAST LLLYQELMRKGIRWLIELIKDDYNETVHKKTEVVITLGFLVSR
84	823	1	314	GTRKMGPTVSPICLPGTWGDYNLMDGDLGLISGWGRTEKRDRA DRLKAGRSPAAG*RKWEPGRGDPTWEESEEDVHKSKWTRCVDE KGA*C*TDNKRPLRCGVT
85	824	3	302	HELENLIKSAHSYSLY*G*YLHGA*TAEPEASFCPRRGWNRQA GAAGSRMNFRPGVLSSRQLGLPGPPDGPDYTVYYPFHRLAMVT AASRLEREHLTHL
86	825	87	422	PVPLPHPILEVCPGQ*EPQSAISLTAFQVQAGASRASPGPPAP SSSKPGRKAKVASPCPDRPAPPPT*PRPAAAPGSESSPRPPRP RTGRRQQRAHARRAAARTAPWRPSC
87	826	3	289	HEGRRRGWASASQRFLRNWAFLTPSKVRRLKGQKAFGKLPSHS DTSLTSDLGFHHRFNPNASSSFKPSGTKFAIQYGTGRVDGILS EDKLTVSGL
88	827	1	101	GRNIMHYPNGHAICIANGHCIIL*NSHNIKVWV

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89	828	1	535	INLGNTCYMNSVI*ALFMATDFRRQVLSLNLNGCNSLMKKLQH LFAFLAHTQREAYAPRIFFEASRPPWFTPRSQQDCSEYLRFLL DRLHEEEKILKVQASHKPSEILECSETSLQEVASKAAVLTETP RTSDGEKTLIEKMFGGKLRTHIRCLNCTSTSQKVEAFTDLSLA FWPSSS
90	829	1	434	ARDDPRVRLSLSPNFF*LASKLGKQWTPLIILANSLSGTNMGE
91	830	3	782	MHRIKLNDRMTFPEELDMSTFIDVEDEKSPQTESCTDSGAENE GSCHSDQMSNDFSNDDGVDEGICLETNSGTEKISKSGLEKNSL IYELFSVMVHSGSAAGGHYYACIKSFSDEQWYSFNDQHVSRIT QEDIKKTHGGSSGSRGYYSSAFASSTNAYMLIYRLKDPARNAK FLEVDEYPEHIKNLVQKERELEEQEKRQREIERNTCKIKLFCL HPTKQVMMED*IEVHKDKTLKEAVEMAYKMMDLEEVIPLDCCR L
92	831	2	604	SVMPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHG TLQLGQALNGVYRTTEGRLTKARNSLGLYGRTIELLGQEVSRG RDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQKVLR DSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHV QRQRREMVAQQHRLRQIQERLHTAALPA
93	832	16	690	ITSVDPRVRGNASTGYGKIWLDDVSCDGDESDLWSCRNSGWGN NDCSHSEDVGVICSDASDMELRLVGGSSRCAGKVEVNVQGAVG ILCANGWGMNIAEVVCRQLECGSAIRVSREPHFTERTLHILMS NSGCAGGEASLWDCIRWEWKQTACHLNMEASLICSAHRQPRLV GADMPCSGRVEVKHAHTWRSVCDSDFSLHAANVLCRELNCGDA ISLSVGDHFG
94	833	108	727	SNYPSSRFRVAGITGVKLGMRSIPIATACTIYHKPFCETNLDA YDPYLIAMSSIYLAGKVEEQHLRTRDIINVSNRYFNPSGEPLE LDSRFWELRDSIVQCELLMLRVLRFQVSFQHPHKYLLHYLVSL QNWLNRHSWQRTPVAVTAWALLRDSYHGALCLRFQAQHIAVAV LYLALQVYGVEVPAEVEA/DEAVGWQIYAMDTEIP
95	834	118	376	RGSRHAVHGWAFGLLFINKESVVMAYLFTTFNAFQGVFIFVFH CALQKKVRSRRGPGSQPPLETFPGYPGEGGEGGGDSGAPSSPQ
96	835	3	333	ARKDDLPPNMRFHEEKRLDFEWTLKAG*EKG*PSK*NKGWEGQ E***TVRD*GIS**VKPQHLS*\ALQMALKRVYTLLSSWNCLE DFDQIFWGQKSALAGQWFPEVSIIP
97	836	740	951	GKQQRETLRRPSPTISVQRAGSPEHSSASH*HSPCPAPGQRVL PTALCTLMTSKHFHGCPLAGQGRAVTL

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98	837	81	1503	GVCGLPRFCGSIILCHYEMSSLGASFVQIKFDDLQFFENCGGG SFGSVYRAKWISQDKEVAVKKLLKIEKEAEILSVLSHRNIIQF YGVILEPPNYGIVTEYASLGSLYDYINSNRSEEMDMDHIMTWA TDVAKGMHYLHMEAPVKVIHRDLKSRNVVIAADGVLKICDFGA SRFHNHTTHMSLVGTFPWMAPEVIQSLPVSETCDTYSYGVVLW EMLTREVPFKGLEGLQVAWLVVEKNERLTIPSSCPRSFAELLH QCWEADAKKRPSFKQIISILESMSNDTSLPDKCNSFLHNKAEW RCEIEATLERLKKLERDLSFKEQELKERERRLKMWEQKLTEQS NTPLLLPLAARMSEESYFESKTEESNSAEMSCQITATSNGEGH GMNPSLQAMMLMGFGDIFSMNKAGAVMHSGMQINMQAKQNSSK TTSKRRGKKVNMALGFSDFDLSEGDDDDDDDGEEEYNDMDNSE
99	838	185	328	MLWETGCSAACRVTVSPTVTFATFSTRGIDAMRPGPSFLWRQQ LSQG*
100	839	1	348	PTLGDQPDLHSITRASRPKLCTRKNCNPLTITVHDPNSTQ*YY GMSWELRFYIPGFDVGTMFTIQKILVSWSPPKPIGPLTDLGDP MFQKPPNKVDLTVPPPFLVIKDTLQKFEKI
101	840	1	416	SLNNVTLPQAKTEKDFIQLCTPGVIKQEKLGTVYCQASSPGAN MIGNKMSAISVHGVSTSGGQMYHYDMNTASLSQQ*DQKPIFNV IPPIPVGSENWNRCQGSGDDNLTSLGTLNFPGRTVSFSFEMES RSVAQAGVQ
102	841	105	354	RHTQECRCPHTHIHTHTHSHTHSHTHSHSHSHTTPRCSHTQPP HAQAPALC*S*EDRGQPTWKLCAHRPRLKVIKEGGWLGG
103	842	171	347	NYSLSVYLVRQLTAGTLLQKLRAKGIRNPDHSRALSE*HLSSL PHLIWIQVFLALQPS
104	843	2	690	ATYIVDFGFSTTFREGQMLTAFCGMYPYVAPERSLGQACQ*PA RDIQSLSVILYFRNTVGRRARTLPFYS/AEASKLQEKILTGRY HAPPLLALQLDSL/IKLLMLNARKCPSL*LMKNPWVKSSQKMP LIPYEEPL/RGPPQTIQLMVAMGFQAKNISVAIIERKFNYPMA TYLILEHTKQERKCSTIRELSLPPGVPTSPSPSTELSTFPLSL MRAHREPAFNVQPPEESQ
105	844	2	777	AKQELAKLMRIEDPSLLNSRVLLHHAKAGTIIARQGDQDVSLH FVLWGCLHVYQRMIDKAEDVCLFVAQPGELVGQLAVLTGEPLI FTLRAQRDCTFLRISKSDFYEIMRAQPSVVLSAAHTVAARMSP FVRQMDFAIDWTAVEAGRALYRCSSHRAAQARPRGGDLGVVRP C*PPRPLRQGDRSDCTYIVLNGRLRSVIQRGSGKKELVGEYGR GDLIGVVSATPTH*PLAFSRPVPRQLTRIIPGNPGSGEVFPGA
106	845	3	709	HASGWTPGTTQTLGQGTAWDTVASTPGTSETTASAEGRRTPGA TRPAAPGTGSWAEGSVKAPAPIPESPPSKSRSMSNTTEGVWEG TRSSVTNRARASKDRREMTTTKADRPREDIEGVRIALDAAKKV LGTIGPPALVSETLAWEILPQATPVSKQQSQGSIGETTPAAGM WTLGTPAADVWILGTPAADVWTSMEAASGEGSAAGDLDAATGD RGPQATLSQTPAV*PWGPPG

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107	846	3	406	AGTSGTGDTGPGNTAVSGTPVVSPGATPGAPGSSTPGEADIGN TSFGKSGTPTVSAASTTSSPVSKHTDAASATAVTISGSKPGTP GTPGGATSGGKITPGIA*PTLDQKSPCFSGYGGYFPVNPHQNP CADSL
108	847	1	565	RAHRCCLPLPSLSCEIQIGFS*SSIFPGQ*ACPCSCCRSCRRN WPQSPRCPHHPPAPCSLLLSSCLPPPLSCSWRGTSGKPPSQSP AASRSMRPRCSPRTSSLRGASCRGPGGSAPAAASGPRCRGCSR SPRRCSRSGCAAASPPRSQRRSPPLSPPPFPTSGTLLLKTSRF GSATRE*SSPRPRPRP
109	848	2	987	DDVPPPAPDLYDVPPGLRRPGPGTLYDVPRERVLPPEVADGGV VDSGVYAVPPPAEREAPAEGKRLSASSTGSTRSSQSASSLEVA GPGREPLELEVAVEALARLQQGVSATVAHLLDLAGSAGATGSW RSPSEPQEPLVQDLQAAVAAVQSAVHELLEFARSAVGNAAHTS DRALHAKLSRQLQKMEDVHQTLVAHGQALDAGRGGSGATLEDL DRLVACSRAVPEDAKQLASFLHGNASLLFRRTKATAPGPEGGG TLHPNPTDKTSSIQSRPLPSPPKFTSQDSPDGQYENSEGGWME DYDYVHLTGGRRSF*KTQKELLGKRAA
110	849	84	372	MATDEENVYGLEENAQSRQESTRRLILVGRTGAGKSATGNSIL GQRRFFSRLGATSVTRACTTGSRRWDKCHVEVVDTPDIFSSQV SKTDPGCEERX*
111	850	2	47	TLGLRSLTKEGGGGGDVAAFEVGTGAAASRALGQCGQLQKLIV IFIGSLCGLCTKCAVSNDLTQQEIQTPEIQQRNA*CDSRVTFT NEGGRWWG
112	851	1192	1040	FFFLVETRFHHIGQAGLELLTLSIK*SARLGLPKCWDDRREPP YLAGFMI
113	852	791	362	RRSPPPAPPPLPSPLSPPPRAPVSPASTMPILLFLIDTSASMN QRSHLGTTYLDTAKGAVETFMKLRARDPASRGDRYMLVTFEEP PYAIKAGWKENHATFMNELKNLQAEGLTTLGQSLRTAFDLLNL NRLVTGIDNYGQVG
114	853	812	348	NCRTYVFCFVLVFRLLFLHGSPLSPSLLSRAGLLCGSAENPTP FLCGITMAAGVSLLALVVRVILSTAILCPSGASRRQRSSEVEW GTDSGVYRLYCWRVGFLGPGGELRLGLSEARGGRVWGRGEKRC RVWAVRSLRKGFGSVAALRRGIWAG
115	854	93	170	VTPTPPQYYTCSCVLGFIACSIFLQMSLKPKVMLLTVALVACL VLFNLSQCWQRDCCSQGLGNLTEPSGTNR*GPAAVSWASLPAP SSCR
116	855	1	183	GKAGGAAGLFAKQVQKKFSRAQEK*TRRFGKTCQPEERAREER QEGPEIEFGFSFFSLSLY

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117	856	53	2400	PKRLFLFQDVNTLQGGGQPVVTPSVQPSLQPAHPALPQMTSQA PQPSVTGLQAPSAALMQVSSLDSHSAVSGNAQSFQPYAGMQAY AYPQASAVTSQLQPVRPLYPAPLSQPPHFQGSGDMASFLMTEA RQHNTEIRMAVSKVADKMDHLMTKVEELQKHSAGNSMLIPSMS VTMETSMIMSNIQRIIQENERLKQEILEKSNRIEEQNDKISEL IERNQRYVEQSNLMMEKRNNSLQTATENTQARVLHAEQEKAKV TEELAAATAQVSHLQLKMTAHQKKETELQMQLTESLKETDLLR GQLTKVQAKLSELQETSEQAQSKFKSEKQNRKQLELKVTSLEE ELTDLRVEKESLEKNLSERKKKSAQERSQAEEEIDEIRKSYQE ELDKLRQLLKKTRVSTDQAAAEQLSLVQAELQTQWEAKCEHLL ASAKDEHLQQYQEVCAQRDAYQQKLVQLQEKSVCFA\CLALQA QITALTKQNEQHIKELEKNKSQMSGVEAAASDPSEKVKKIMNQ VFQSLRREFELEESYNGRTILGTIMNTIKMVTLQLLNQQEQEK EESSSEEEEEKAEERPRRPSQEQSASASSGQPQAPLNRERPES PMVPSEQVVEEAVPLPPQALTTSQDGHRRKGDSEAEALSEIKD GSLPPELSCIPSHRVLGPPTSIPPEPLGPVSMDSECEESLAAS PMAAK\PDNPSGK\VCVQGK*APDGPTYKE\SSTRLFPGFQDP E\EGDPLALGLE\SPG\EPQPPQLQGKVDVH*VPPVPHKGAFQ EQEGRFPQFCRE
118	857	1	791	SETAQQIIDRLRVKLAKEPGANLFLMAVQDIRVGGRQSNASYQ YTLLSDDLAALREWEPKIRKKLATLPELADVNSDQQDNGAEMN LVYDRDTMARLGIDVQAANSLLNNAFGQRQISTIYQPMNQYKV VMEVDPRYTQDISALEKMFVINNEGKAIPLSYFAKWQPANAPL SVNHQGLSAALTISFNLPTGKSLSDASAAIDRAMSQLGVPSTV RGSFAGPAQVFQETMNSQVILIIAAIATVYIVLGIPYERYVHP PTILL*RPGANLFLMAVQDIRVGGRQSNASYQYTLLSDDLAAL REWEPKIRKKLATLPELADVNSDQQDNGAEMNLVYDRDTMARL GIDVQAANSLLNNAFGQRQISTIYQPMNQYKVVMEVDPRYTQD ISALEKMFVINNEGKAIPLSYFAKWQPANAPLSVNHQGLSAAL TISFNLPTGKSLSDASAAIDRAMSQLGVPSTVRGSFAGPAQVF QETMNSQVILIIAAIATVYIVLGIPYERYVHPPTILL
119	858	3	417	IITPDAMGCQKDIAEKIQKQGGDYLFAVKGNQGRLNKAFEEKF PLKELNNPEHDSYAISEKSHGREEIRLHIVCDVPDELIDFTFE WKGLKKLCVAVSFRSIIAEQKKEPEMTVRYNIS*LGIAGDISV TAISGTDD
120	859	2	373	HYLKMLTQARREVIIANAYFFPGYRFLHALRKAARRGVRIKLI IQGEPDMPIVRVGARLLYNYLVKGGVQVFEYRRRPLHGKVALM DDHWATVGSSNLHPVS*SGNLQANVILHVLRVPTLNP
121	860	286	495	CWSKSAAFHSKLATTCIVPVCAAGHCSAAW*SLRPIEALAKEV RELK*HTR*LLNPATTRELTSLGRNLNRLLKSERERYDKYRTT LTDLTHSLKTPLAVLQSTLRSLRSEKMSVSDAEPVMLEQISRI SQQIGYYLHRASMRGGTLLSRELHPVAPLLDNLTSALIKGKPR KGGNVTVFPFTAMYRDGH

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122	861	2	725	GNTVMFQHLMQKRKHTQWTYGPLTSTLYDLTEIDSSGDEQSLL ELIITTKKREARQILDQTPVKELVSLKWKRYGRPYFCMLGAIY LLYIICFTMCCIYRPLKPRTNNRTSPRDNTLLQQKLLQEAYMT PKDDIRLVGELVTVIGAIIILLVEVPDIFRMGVTRFFGQTILG GPFHVLIITYAFMVLVTMVMRLISASGEVVPMSFALVLGWCNV MYFARGFQMLGPFTIMIQKMIFGDLM
123	862	1	135	EKAAAANIDEVQKSDVSSTGQGVIDKDALGPMMLEVAHLHFSA VF
124	863	2	364	LEVPSEVTPLGFAMQATKTLLLRTCCLQEFNIMEKNKGWALLG GKDGHLQGLFLLANALLERNQLLAQKVMYLLVPLLNRGNDKHK LTSAGFFVELLRSPVAKRLPSIYSVARFKDWLQD
125	864	1	374	RPAPAPSAAPEEAPSP\GVKGRGMAKRRVPAPVWGGAGGGTKS ARRAAAAPDTERSEEGGRAVKEAYPSSRQPPPPSP*PLRCARR CHPNLAPSMPISNREGKGKRREEKIRPLSPASTHTSARA
126	865	3	364	LQGVHGSSSTFCSSLSSDFDPLEYCSPKGDPQRVDMQPSVTSR PRSLDSEVPTGETQVSSHVHYHRHRHHHYKKRFQRHGRKPGPE TGVPQSRPPIPRTQPQPEPPSPDQQVTRSNSAAP
127	866	2	250	MADPDPRYPRSSIEDDFNYGSSEASDTVHIRMAFLRRVYSILS LQDLLATVTSTDNLAFEDGRTDWLQRPDCVSFKIHVLPM
128	867	194	375	AGMSVVVVPPIGSSYLGLISQEHFPNEFTSGDGKKAHQDFGYF YGSSYVAASDSSRTPGL
129	868	104	339	VAAALTLFPQQLSPPGAWGLGLSACFCCAEGFSRLNQQVLSSS LLLLSRTNCPCKYSFLDNLKKLTPRRDVPTYPKVR
130	869	2	360	RDDACLYSPASAPEVITVGATNAQDQPVTLGTLGTNFGRCVDL FAPGEDIIGASSDCSTCFVSQSGTSQAAAHVAGIAAMMLSAEP ELTLAELRQRLIHFSAKDVINEAWFPEDQRVLT
131	870	2	105	LEIKFLEQVDQFYDDNFPMEIRHLLAQWIENQDW
132	871	2	466	EAGDADEDEADANSSDCEPEGPVEAEEPPQEDSSSQSDSVEDR SEDEEDEHSEEEETSGSSASEESESEEESEDAQSQSQADEEEED DDFGVEYLLARDEEQSEADAGSGPPTPGPTTLGPKKEITDIAA AAESLQPKGYTLATTQVKTPIPLLL
133	872	1	354	LKNLRELLLEDNQLPQIPSGLPESLTELSLIQTNIYNITKEGI SRLINLKNLYLAWNCYFNKVCEKTNIEDGVFETLTNLELLSLS FNSLSHVPPKLPSSLRKLFLSNTQIKYISEED
134	873	59	184	MRSQALGQSAPSLTASLKELSLPRRGSFPVCPNAGRTSPLG*
135	874	1	210	LLCVCLPVGACPSLSLLTAPLNQLMRCLRKYQSRTPSPLLHSV PSEIVFDFEPGPVFRGSWALLSWSTRP
136	875	131	254	QTPDKKQNDQRNRKRKAEPYETSQGSNNFVSTKVLNSNVLR
137	876	84	504	YFIIKGMVELVPASDTLRKIQVEYGVTGSFKDKPLAEWLRKYN PSEEEYEKASENFIYSCAGCCVATYVLGICDRHNDNIMLRSTG HMFHIDFGKFLGHAQMFGSFKRDRAPFVLTSDMAYVINGGEKP TIRFQLFVDL

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138	877	3	215	PSPLPSLSLPPPVAPGGQESPSPHTAEVESEASPPPARPLPGE ARLAPISEEGKPQLVGRF\QVTSSK\NRLSLFPCSQHPPLSLV LQNLQPLSSLQRAQIQRTV/PGGGPETREALAESDRAAEGLGA GVEEEGDDGKEPQVGGSPQPLSHPSPVWMNYSYSSLCLSSEES ESSGEDEEFWAELQSLRQKHLSEVETLQTLQKKEIEDLYSRLG KQPPPGIVAPAAMLSSRQRRLSKGSFPTSRRNSLQRSEPPGPG ETA/GHPASIFSLRPLSVDCFSPGPGGLPRGNRPPLPTSPFLT *CSPSPHTAEVESEASPPPARPLPGEARLAPISEEGKPQLVGR FPSDFIQGTG
139	878	1	337	RRFVSQETGNLYIAKVEKSDVGNYTCVVTNTVTNHKVLGPPTP LILRNDGVMGEYEPKIEVQFPETVPTAKGATVKLECFALGNPV PTIIWRRADGKPIARKARRHKSRVGK
140	879	72	917	MLRTCYVLCSQAGPRSRGWQSLSFDGGAFHLKGTGELTRALLV LRLCAWPPLVTHGLLLQAWSRRLLGSRLSGAFLRASVYGQFVA GETAEEVKGCVQQLRTLSLRPLLAVPTEEEPDSAAKSGEAWYE GNLGAMLRCVDLSRGLLEPPSLAEASLMQLKVTALTSTRLCKE LASWVRRPGASLELSPERLAEAMDSGQNLQVSCLNAEQNQHLR ASLSRLHRVAQYARAQHVRLLVDAEYTSLNPALSLLVAALAVR WNSPGEGGPWVWNTYQACLKDTF*
141	880	219	308	PHHRIAGDTAIDKNIHQSVSEQIKKNFAK
142	881	182	317	QMTNPFFLCFTTMISNCNFFKGPPGPPGEKGDRGPTGESGPRG FP
143	882	177	341	NGIIASFFLRTFIFCFIHIQGCQAGQTIKVQVSFDLLSLMFTF VSPCTNDLIIH
144	883	3	1441	KLSVNHRRTHLTKLMHTVEQATLRISQSFQKTTEFDTNSTDIA LKVFFFDSYNMKHIHPHMNMDGDYINIFPKRKAAYDSNGNVAV AFLYYKSIGPLLSSSDNFLLKPQNYDNSEEEERVISSVISVSM SSNPPTLYELEKITFTLSHRKVTDRYRSLCAFWNYSPDTMNGS WSSEGCELTYSNETHTSCRCNHLTHFAILMSSGPSIGIKDYNI LTRITQLGIIISLICLAICIFTFWFFSEIQSTRTTIHKNLCCS LFLAELVFLVGINTNTNKLFCSIIAGLLHYFFLAAFAWMCIEG IHLYLIVVGVIYNKGFLHKNFYIFGYLSPAVVVGFSAALGYRY YGTTKVCWLSTENNFIWSFIGPACLIILVNLLAFGVIIYKVFR HTAGLKPEVSCFENIRSCARGALALLFLLGTTWIFGVLHVVHA SVVTAYLFTVSNAFQGMFIFLFLCVLSRKIQEEYYRLFKNVPC CFGCLR
145	884	1	429	GTREAAPSRFMFLLFLLTCELAAEVAAEVEKSSDGPGAAQEPT WLTDVPAAMEFIAATEVAVIGFFQDLEIPAVPILHSMVQKFPG VSFGISTDSEVLTHYNITGNTICLFRLVDNEQLNLEDEDIESI DATKLSRFIEINSL
146	885	1	156	DETSGLIVREVSIEISRQQVEELFGPEDYWCQCVAWSSAGTTK SRKAYVRIA
147	886	1	121	GTRSIHVKLDVGKLHTQPKLAAQLRMVDDGSGKVEGLPGI

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
148	887	128	652	XCGEDGSFTQVQCHTYTGYCWCVTPDGKPISGSSVQNKTPVCS GSVTDKPLSQGNSGRKDDGSKPTPTMETQPVFDGDEITAPTLW IKHLVIKDSKLNNTNIRNSEKVYSCDQERQSALEEAQQNPREG IVIPECAPGGLYKPVQCHQSTGYCWCVLVDTGRPLPGTSTRYV MPSX*
149	888	128	273	VLQLIKSQKFLNKLVILVETEKEKILRKEYVFADSKVSDSKLL KWAVR
150	889	1	948	RRLSLLDLQLGPLGRDPPQECSTFSPTDSGEEPGQLSPGVQFQ RRQNQRRFSMEDVSKRLSLPMDIRLPQEFLQKLQMESPDLPKP LSRMSRRASLSDIGFGKLETYVKLDKLGEGTYATVFKGRSKLT ENLVALKEIRLEHEEGAPCTAIREVSLLKNLKHANIVTLHDLI HTDRSLTLVFEYLDSDLKQYLDHCGNLMSMHNVKVRPRGQGPP ILAATCPEAQCGDPLSPPGIRLLRWLKPSHVGKRERAMPSTSP GTGLSALPQEQTHTVCHCLAVGIKPTLNSEHQFPSLSNGSVSY LPKCREASGEARGYE
151	890	3	108	HERHEPSPTALAFGDHPIVQPKQLSFKIIQVNDN
152	891	2	208	ARGPSLLSEFHPGSDRPQERRTSYEPIHPGPSPVDHDSLESKR PRLEQASDSHYQGHITGESLPGRVH
153	892	1	116	GTRKEEFSAEENFLILTEMATNHVQVLVEFTKKLPGIF
154	893	74	661	HTHKLVAPRPGLPPTSQWPRDAGRQASGGLPSLSTGPPKGPRD GLARGHPAEWLAGSPGNNSPTQGSLPPQLDLYAGALFVHICLG WNFYLSTILTLGITALYTIAGMVPAAGRSTQGTCKGVRRPPPP TGPREQPRKWPQQEPQKFLPVSLLPGARAPSSNLASTGRGPGC CNLHGRPADAHHGGGGCHPDNQR
155	894	55	312	MVNHSLQETSEQNVILQHTLQQQQQMLQQETIRNGELEDTQTK LEKQVSKLEQELQKQRESSAEKLRKMEEKCESAAHEADLKRQK *
156	895	38	185	VCPKWCRFLTMLGHCCYFWHVWPAS*ALSAGPTPTSRSFSPSP LRSIST
157	896	37	462	MRGPPVLLLQAAPMECPVPQGIPAGSSPEPAPDPPGPHFLRQE RSFECRMCGKAFKRSSTLSTHLLIHSDTRPYPCQFCGKRFHQK SDMKKHTYIHTGEKPHKCQTQREPTMVLSPADKTNVKAAWX*
158	897	3	175	HEQLTNNTATAPSATPVFGQVAASTAPSLFGQQTGITASTAVA TPQVISSRFINLDF
159	898	187	677	VSVFKNCPMY*ICIFLTKMFCVLII*NKF*VHKKPLQEVEIA AITHGALQGLAYLHSHTMIHRDIKAGNILLTEPGQVKLADFGS ASMASPANSFVGTPYWMAPEVILAMDEGQYDGKVDVWSLGITC IELAERKPPLFNMNAMSALYHIAQNESPTLQSNEW

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160	899	2	1060	RHARPGGGGHSNQRKMSLEQEEETQPGRLLGRRDAVPAFIEPN VRFWITERQSFIRRFLQWTELLDPTNVFISVESIENSRQLLCT NEDVSSPASADQRIQEAWKRSLATVHPDSSNLIPKLFRPAAFL PFMAPTVFLSMTPLKGIKSVILPQVFLCAYMAAFNSINGNRSY TCKPLERSLLMAGAVASSTFLGVIPQFVQMKYGLTGPWIKRLL PVIFLVQASGMNVYMSRSLESIKGIAVMDKEGNVLGHSRIAGT KAVRETLASRIVLFGTSALIPEVFTYFFKRTQYFRKNPGSLWI LKLSCTVLAMGLMVPFSFSIFPQIGQIQYCSLEEKIQSPTEET EIFYHRGV
161	900	3	564	HASGRLEVFYNGTWGSVGRRNITTAIAGIVCRQLGCGENGVVS LAPLSKTGSGFMWVDDIQCPKTHISIWQCLSAPWERRISSPAE ETWITCEDRIRVRGGDTECSGRVEIWHAGSWGTVCDDSWDLAE AEVVCQQLGCGSALAALRDASFGQGTGTIWLDDMRCKGNESFL WDCHAKPWGQSDCG
162	901	1099	2	LGDFPQPQRQRRPGASDLPPHLAGARQWEVRFFRHLPARTLPP SLRMPEGPELHLASQFVNEACRALVFGGCVEKSSVSRNPEVPF ESSAYRISASARGKELRLILSPLPGAQPQQEPLALVFRFGMSG SFQLVPREELPRHAHLRFYTAPPGPRLALCFVDIRRFGRWDLG GKWQPGRGPCVLQEYQQFRENVLRNLADKAFDRPICEALLDQR FFNGIGNYLRAEILYRLKIPPFEKARSVLEALQQHRPSPELTL SQKIRTKLQNPDLLELCHSVPKEVVQLGGRGYGSESGEEDFAA FRAWLRCYGMPGMSSLQDRHGRTIWFQGDPGPLAPKGRKSRKK KSKATQLSPEDRVEDALPPSK
163	902	3	335	LTWSACYWRDILRIQLWIAADILLRMLEKALLYSEHQNISNTG LSSQGLLIFAELIPAIKRTLARLLVIIASLDYGIEKPHLGTGM HRVIGLMLLYLIFANAESVIRVIG
164	903	2	135	FFFEMESRSAAQAGVQWCNLGSLQALPPRFTPFSCLSLPSSWD Y
165	904	74	645	YECEELAKKLENSQRDGISRNKLALAELYEDEVKCKSSKSNRP KATVFKSPRTPPQRFYSSEHEYSGLNIVRPSTGKIVNELFKEA REHGAVPLNEATRASGDDKSKSFTGGGYRLGSSFCKRSEYIYG ENQLQDVQILLKLWSNGFSLDDGELRPYNEPTNAQFLESVKRG VTLIACMPEIQQLMLEIF
166	905	14	1257	WPCGAAPGLTHASERMFTLTTMIQALAPVMGWDRKPLKMFSSE EMRGHLHHHHKCLTKILKVEGQVPDLPSCLPLTDNTRMLASIL INMLYDDLRCDPERDHFRKICEEYITGKFDPQDMDKNLNAIQT VSGILQGPFDLGNQLLGLKGVMEMMVALCGSERETDQLVAVEA LIHASTKLSRATFIITNGVSLLKQIYKTTKNEKIKIRTLVGLC KLGSAGGTDYGLRQFAEGSTEKLAKQCRKWLCNMSIDTRTRRW AVEGLAYLTLDADVKDDFVQDVPALQAMFELAKTSDKTILYSV ATTLVNCTNSYDVKEVIPELVQLAKFSKQHVPEEHPKDKKDFI DMRVKRLLKAGVISALACMVKADSAILTDQTKELLARVFLALC DNPKDRGTIVAQGGGKALIPLALEGTD

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167	906	3	894	VDSVGGGSESRSLDSPTSSPGAGTRQLVKASSTGTESSDDFEE RDPDLGDGLENGLGSPFGKWTLSSAAQTHQLRRLRGPAKCREC EAFMVSGTECEECFLTCHKRCLETLLILCGHRRLPARTPLFGV DFLQLPRDFPEEVPFVVTKCTAEIEHRALDVQGIYRVSGSRVR VERLCQAFENGRALVELSGNSPHDVSSVLKRFLQELTEPVIPF HLYDAFISLAKTLHADPGDDPGTPSPSPEVIRSLKTLLVQLPD SNYNTLRHLVAHLFRVAARFMENKMSANNLGIVFGPTL
168	907	1	394	GLHVISLHSADGRHWEDPLSELDSERVSAFLVTETLVFYLFCL LADETVVPPDVPSYLSSQGTLSDRQETVVRTEGGPQANGHIES NGKASVTVKQSSAVTVSLGAGGGLQVFTGQVPGIRWGKLGEAH AS
169	908	179	551	KIKHRPEEEPRWAAAGAQSAGPGAAEVAPPRPGTVAPGANGMT DSATANGDDRDPEIELFVKAGIDGESIGNCPFSQRLFMILWLK GVVFNVTTVDLKRKPADLRNLAPGTHPPFLAFNWYVKT
170	909	1	335	LGFSDGQEARPEEIGWLNGYNETTGERGDFPGTYVEYIGRKKI SPPTPKPRPPRPLPVAPGSSKTEADVEQQVLYKYRKKPSSSHR PQTPHNGKSKNFLHKQGLKKKKASL
171	910	1	895	RTRGVMELALRRSPVPRWLLLLPLLLGLNAGAVIDWPTEEGKE VWDYVTVRKDAYMFWWLYYATNSCKNFSELPLVMWLQGGPGGS STGFGNFEEIGPLDSDLKPRKTTWLQAASLLFVDNPVGTGFSY VNGSGAYAKDLAMVASDMMGLLKTFFSCHKEFQTVPFYIFSES YGGKMAAGIGLELYKAIQRGTIKCNFAGVALGDSWISPVDSVL SWGPYLYSMSLLEDKGLAEVSKVAEQVLNAVNKGLYREATELW GKAEMIIEQVKRGNTQRRACLAFSGGYRAHGWCCQTWSLH
172	911	553	194	PGWSRSPDLVIRLPRPPKVLGLQYYHFFFFLRWSL/DSVAQAE VQWHDLRSLQAPPPGFTPFSCLSLPGSWDYRCPPPRPANFLYF **RRGFTVLARMVSIS*PRDPPASASQSAGITVLSLFFFFEME SCSVAQAGVQWRYLGSLQALPPGFTPFSCLSLPSSWDYRRPPP RPANFFVFLVETGVSPC*PGWSRSPDLVIRLPQPPKVLGLQV
173	912	1761	1	PSMKTGELEKETAPLRKDADSSISVLEIHSQKAQIEEPDPPEM ETSLDSSEMAKDLSSKTALSSTESCTMKGEEKSPKTKKDKRPP ILECLEKLEKSKKTFLDKDAQRLSPIPEEVPKSTLESEKPGSP EAAETSPPSNIIDHCEKLASEKEVVECQSTSTVGGQSVKKVDL ETLKEDSEFTKVEMDNLDNAQTSGIEEPSETKGSMQKSKFKYK LVPEEETTASENTEITSERQKEGIKLTIRISSRKKKPDSPPKV LEPENKQEKTEKEEEKTNVGRTLRRSPRISRPTAKVAEIRDQK ADKKRGEGEDEVEEESTALQKTDKKEILKKSEKDTNSKVSKVK PKGKVRWTGSRTRGRWKYSSNDESEGSGSEKSSAASEEEEEKE SEEAILADDDEPCKKCGLPNHPELILLCDSCDSGYHTALPFAP PLMIHPQMGGW\F\CPTFCPTLNLLLLEKLEDQF\QDL\DVAL KKERALPERRK\ERLVYVGI\SIENIIPPQ\EPDFSEDQEEKK KDSKKSKANLL\ERRSTRTRKCISYRFDEFDEAIDEAIEDDIK EADGGGVGRGKDISTITGHRGKDISTILDEER

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174	913	3	539	KRRGSFKMAELDQLPDESSSAKALVSLKEGSLSNTWNEKYSSL QKTPVWKGRNTSSAVEMPFRNSKRSRLFSDEDDRQINTRSPKR NQRVAMVPQKFTATMSTPDKKASQKIGFRLRNLLKLPKAHKWC IYEWFYSNIDKPLFEGDNDFCVCLKESFPNLKTRKLTRVEWGK IRRLMG
175	914	166	635	MPEYLRKRFGGIRIPIILAVLYLFIYIFTKISVDMYAGAIFIQ QSLHLDLYLAIVGLLAITAVYTVAGGLAAVIYTDALQTLIMLI GALTLMGYSFAAVGGMEGLKEKYFLALASNRSENSSCGLPRED AFHIFRDPLTSDLPWPGVLFGMSIPSLX*
176	915	673	1025	XSASATSLTLSHCVDVVKGLLDFKKRRGHSIGGAPEQRYQIIP VMCCSLLATGGADRLIHLWNVVGSRLEANQTLEGAGGSITSVD FDPSGYQVLAATYNQVAQFWK*
177	916	3	139	QKRFPSNCGRDGKLFLWGQALHIIAKLLGKWRRLGMVFFSLLL SY
178	917	1	541	VHVCSSKMGALSTERLQYYTQELGVRERSGHSVSLIDLWGLLV EYLLYQEENPAKLSDQQEAVRQGQNPYPIYTSVNVRTNLSGED FAEWCEFTPYEVGFPKYGAYVPTELFGSELFMGRLLQLQPEPR ICYLQGMWGSAFATSLDEIFLKTAGSGLSFLEWYRGSVNITDD CQKPQLHN
179	918	1	628	EFLGRPTRPAKDEGNDEGKDEGKDEGKDEGKDEGKDEGKDERK DEGKDEGKDERKDEGKDEGKDEGKDEGKDEGKDEGKDEGKDEG NDEGKDEGKDEGKDEGKDEGKDEGKDERKDEGKDEGKDERKDE GKDEGKDEGKDEGKDEGKDEGKDEGKDEGNDEGKDEGKDEGKD EGKDEGKDEGKDEGNDEGNDEGNDEGKDEGKDERNDEGKDEGK DEGKDEGKDERNDEGKDERKDEGKDEGKDEGKDEGKDEGKDEG NDEGKDERKDEGKDEGKDEGKDK
180	919	27	471	PSLRPAWHEGEDFSYGLQPYCGYSFQVVGEMIRNREVLPCPDD CPAWAYALMIEGWNEFPSRRARFKDIHSRLRAWGNLSNYNSSE QTSGGRNTTQTSSLSTSPLCNVSNAPYVGPKQKVPPFPQTQVI PMKGQIRPMVPPPQLYVP
181	920	2	454	RNSGRHPRVRWILEERKRVMQEACAKYRASSSRRAVTPRHVSR IFVEDRHRVLYCEVPKAGCSNWKRVLMVLAGLASSTADIQHNT VHYGSALKRLDTFDRQGILHRLSTYTKMLFVREPFERLVSAFR DKFEHPNSYYHPVFCMAILAR
182	921	2	378	IMYSISPANSEEGQELYVCTVKDDVNLDTVLLLPFLKEIAVSQ LDQLSPEEQLLVKCAAIIGHSFHIDLLQHLLPGWDKNKLLQVL RALVDIHVLCWSDKSQELPAEPILMPSSIDIIDGTKEKK
183	922	181	513	GPHVVLVLRRCFLLSYFKGVEKAKAMPSPRILKTHLSTQLLPP SFWENNCKVRYQQLPVTEGKVSQPKRVLQTPTQSIRDHLCLST VSDAYQQRENIKFYIQQDIHLNSFK
184	923	32	239	FYYICRLSKEDKAFLWEKRYYCFKHPNCLPKILASAPNWKWVN LAKTYSLLHQWPALYPLIALELLDSK

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185	924	3	361	KMMI*GLFEIQQCPIGKHCNFLQVLRN/PNRDL/WLVSSFGKS SKGRERMGHHDEYYRLRGR/HNPSPDHSYKRNGESERKRKKSH *HMSKSQERHNSPSRGRNSDRSGGRCSRSDNGRSRYR
186	925	443	1412	PLSLFARVAGSRVEMPEPPGLGDEGRPLLHPGRREAVGSWVSA FAGDSTPCGPGDLSVPRREPFRLTAL*PHRSPVVRTSLIGLLL GFSVKEELRGVGWAARTPLGIR
187	926	2	917	FDKRQHEARIQQMENEIHYLQENLKSMEEIQGLTDLQLQEADE EKERILAQLRELEKKKKLEDAKSQEQVFGLDKELKKLKKAVAT SDKLATAELTIAKDQLKSLHGTVMKINQERAEELQEAERFSRK AAQAARDLTRAEAEIELLQNLLRQKGEQFRLEMEKTGVGTGAN SQVLEIEKLNETMERQRTEIARLQNVLYLTGSDNKGGFENVLE EIAELRREGSYQNDYISSMADPFKRRGYWYFMPPPPSSKVSSH SSQATKDSGVGLKYSASTPVRKPRPGQQDGKEGSQPPPASGYW VYSP
188	927	171	1082	SDASSFKTRVIVVPRPRVFPLGSAITENSLESDSQIGQFGVGF YSAFLVADKVIVTSKHNNDTQHIWESDSNEFSVIADPRGNTLG RGTTITLVLKEEASDYLELDTIKNLVKKYSQFINFPIYVWSSK TETVEEPMEEEEAAKEEKEESDDEAAVEEEEEEKKPKTKKVEK TVWDWELMNDIKPIWQRPSKEVEEDEYKAFYKSFSKESDDPMA YIHFTAEGEVTFKSILFVPTSAPRGLFDEYGSKKSDYIKLYVR RVFITDDFHDMMPKYLNFVKGVVDSDDLPLNVSRETLQQHKLL KV
189	928	718	275	CGSWMRRALIPPCRGGPSASDRCCSCSPSGFSAGRGRCPVQGC LRPHRVQLLRRWGPGSPAGQRLSKGFQLLRWWGPGSPAPEPRK GPFPPPDPPWPVTAVTVMAGSVPSAQSVDALESPGPLALEGPS SPRNLLWREMSIFLPGIF
190	929	1	550	PGPTPPPRHGSPPHRLIRVETPGPPAPPADERISGPPASSDRL AILEDYADPFDVQETGEGSAGASGAPEKVPENDGYMEPYEAQK MMAEIRGSKETATQPLPLYDTPYEPEEDGATPEGEGAPWPRES RLPEDDERPPEEYDQPWEWKKERISKAFAVDIKVIKDLPWPPP VGQLDSSPSLP
191	930	1	562	QFFSLFLRYQIHTGLQHSIIRPTQPNCLPLDNATLPQKLKEVG YSTHMVGKWHLGFYRKECMPTRRGFDTFFGSLLGSGDYYTHYK CDSPGMCGYDLYENDNAAWDYDNGIYSTQMYTQRVQQILASHN PTKPIFLYIAYQAVHSPLQAPGRYFEHYRSIININRRRYAAML SCLDEAINNVTLALK
192	931	3	580	RVRKGRGGERLQSPLRVPQKPERPPLPPKPQFLNSGAYPQKPL RNQGVVRTLSSSAQEDIIRWFKEEQLPLRAGYQKTSDTIAPWF HGILTLKKANELLLSTGMPGSFLIRVSERIKGYALSYLSEDGC KHFLIDASADAYSFLGVDQLQHATLADLVEYHKEEPITSLGKE LLLYPCGQQDQLPDYLELFE

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193	932	3	1641	GSLEKALFQLLKVWGQWAEQTRRLQRLDVSLSVARVRSAGPSC QNKGDLVMEALLEGIQNRGHGGGFLTSCEAELQELMKQIDIMV AHKKSEWEGRTHALETCLKIREQELKSLRSQLDVTHKEVGMLH QQVEEHEKIKQEMTMEYKQELKKLHEELCILKRSYEKLQKKQM REFRGNTKNHREDRSEIERLTAKIEEFRQKSLDWEKQRLIYQQ QVSSLEAQRKALAEQSEIIQAQLVNRKQKLESVELSSQSEIQH LSSKLERANDTICANELEIERLTMRVNDLVGTSMTVLQEQQQK EEKLRESEKLLEALQEEKRELKAALQSQENLIHEARIQKEKLQ EKVKATNTQHAVEAISLESVSATCKQLSQELMEKYEELKRMEA HNNEYKAEIKKLKEQILQGEQSYSSALEGMKMEISHLTQELHQ RDITIASTKGSSSDMEKRLRAEMQKAEDKAVEHKEILDQLESL KLENRHLSEMVMKLELGLHECSLPVSPLGSIATRFLEEEELRS HHILERLDAHIEELKRESEKTVRQFTALK
194	933	159	1053	TGFLGWSQGPSLTPTSLSALYPSQVEETGVVLSLEQTEQHSRR PIQRGAPSQKDTPNPGDSLDTPGPRILAFLHPPSLSEAALAAD PRRFCSPDLRRLLGPILDGASVAATPSTPLATRHPQSPLSADL PDELPVGTENVHRLFTSGKDTEAVETDLDIAQDADALDLEMLA PYISMDDDFQLNASEQLPRAYHRPLGAVPRPRARSFHGLSPPA LEPSLLPRWGSDPRLSCSSPSRGDPSASSPMAGARKRTLAQSS KDEDEGVELLGVRPPKRSPSPEHENFLLFPLSLSFLLTG
195	934	3	425	ELQDCFDVHDASWEEQIFWGWHNDVHIFDTKTQTWFQPEIKGG VPPQPRAAHTCAVLGNKGYIFGGRVLQTRMNDLHYLNLDTWTW SGRITINGESPKHRSWHTLTPIADDKLFLCGGLNAYNMPLSDG WIHNVTTHCWK
196	935	2	295	FFFLRTRSHSVTPRWECSDDITAHWQPQPWGSSDPLTFS/RPQ VVVPPRHTTLCP\ANFFVFCIFCRNRISPCWPGWSRTPWAQLI RLPRPPKVLGLQV
197	936	2	737	PREGQVKQGLLGDCWFLCACAALQKSRHLLDQVIPPGQPSWAD QEYRGSFTCRIWQFGRWVEVTTDDRLPCLAGRLCFSRCQREDV FWLPLLEKVYAKVHGSYEHLWAGQVADALVDLTGGLAERWNLK GVAGSGGQQDRPGRWEHRTCRQLLHLKDQCLISCCVLSPRAGE ARGQHGRAAASVPPTARPQAHCSFLCDWLHSPVRTKWEEVSLF SRVVSSVCDLPLLSSSRGTWPFSPLTSPFH
198	937	3	638	AECLEASIARYAHRVANSRYTFDGETVTLSPSQGVNQLHGGPE GFDKRRWQIVNQNDRQVLFALSSDDGDQGFPGNLGATVQYRLT DDNRISITYRATVDKPCPVNMTNHVYFNLDGEQSDVRNHKLQI LADEYLPVDEGGIPHDGLKSVAGTSFDFRSAKIIASEFLADDD QRKVKGYDHAFLLQAKGDGKKVAAHVWSADEKLQLKVYT
199	938	69	425	PLSRFLSKESQEDWGMERQSRVMSEKDEYQFQHQGAVELLVFN FLLILTILTIWLFKNHRFRFLHETGGAMVYDKPPKFAMSREQM SQSCSHTAHNASLLTDAGPLSCGESRASCLFL

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200	939	3	435	DSKEPRLQQLGLLEEEQLRGLGFRQTRGYKSLAGCLGHGPLVL QLLSFTLLAGLLVQVSKVPSSISQEQSRQDAIYQNLTQLKAAV GELSEKSKLQEIYQELTQLKAAVGELPEKSKLQEIYQELTWLK AAVGELPEKSKMQE
201	940	657	469	MQSIAWGHRRDRGESPLGWGQESEASPSALTEAPKAAHTTRLG FLAANNPNGHSQPQDSFLL*
202	941	1	714	FETLSMRGIPHMLALGPQQLLAQDEEGDTLLHLFAARGLRWAA YAAAEVLQVYRRLDIREHKGKTPLLVAAAANQPLIVEDLLNLG AEPNAADHQGRSVLHVAATYGLPGVLLAVLNSGVQVDLEARDF EGLTPLHTAILALNVAMRPSDLCPRVLSTQARDRLDCVHMLLQ MGANHTIQVSGDVGGQTLGDCVEWGHLDVRELQANADFASSLL RALEHVTSLLCALRVFCLFLCQL
203	942	3	479	DAWADAWVGTKMADLDSPPKLSGVQQPSEGVGGGRCSEISAEL IRSLTELQELEAVYERLCGEEKVVERELDALLEQQNTIESKMV TLHRMGPNLQLIEGDAKQLAGMITFTCNLAENVSSKVRQLDLA KNRLYQAIQRADDILDLKFCMDGVQTALR
204	943	1	706	AVEFRVPRSGSAYLYSYVTVGELWAFTTGWNLILSYVIGTASV ARAWSSAFDNLIGNHISKTLQGSIALHVPHVLAEYPDFFALGL VLLLTGLLALGASESALVTKVFTGVNLLVLGFVMISGFVKGDV HNWKLTEEDYELAMAELNDTYSLGPLGSGGFVPFGFEGILRGA ATCFYAFVGFDCIATTGEEAQNPQRSIPMGIGISLSVCFLADF AVSSALTLMMPYYQLQPESP
205	944	1	852	GFHPNTTHYRARAAARAGAGSFVGEVSAVDKDFGPNGEVRYSF EMVQPDFELHAISGEITNTHQFDRESLMRRRGTAVFSFTVIAT DQGIPQPLKDQATVHVYMKDINDNAPKFLKDFYQATISESAAN LTQVLRVSASDVDEGNNGLIHYSIIKGNEERQFAIDSTSGQVT LIGKLDYEATPAYSLVIQAVDSGTIPLNSTCTLNIDILDENDN TPFF/LLNQHFFVDVLENMRIGELGASGTATDS\DSGDIADLY YKFTGTKHPPGTFSISPKHLGVFFLAQK
206	945	3	363	GDCYDLYGGEKFATLAELVQYYMEHHGQLKEKNGDVIELKNPL NCADPTSQRWFHGHLSGKEAEKLLTEKGKHSSFLVRESQSHPG DFVLSVCTGDDKGESNDGKSKVTHVMIHCQELK
207	946	218	717	IDSGNQNGGNDDKTKNAERNYLNVLPGEFYITRHSNLSEIHVA FHLCVDDHVKSGNITARDPAIMGLRNILKVCCTHDITTISIPL LLVHDMSEEMTIPWCLRRAELVFKCVKGFMMEMASWDGGISRT VQFLVPQSISEEMFYQLSNMLPQIFRVSSTLTLTSKH
208	947	3	368	SILPALLVTILIFMDQQITAVIVNRKENKLKKAAGYHLDLFWV GILMALCSFMGLPWYVAATVISIAHIDSLKMETETSAPGEQPQ FLGVREQRVTGIIVFILTGISVFLAPILKCIPLPV
209	948	2	575	GASRVEAGSANGMLIDGGSQIVKVQGHADGTTINKSGSQDVVQ GSLATNTTINGGRQYVEQSTVETTTIKNGGEQRVYESRALDTT IEGGTQSLNSKSTAKNTHIYSGGTQIVDNTSTSDVIEVYSGGV LDVRGGTATNVTQHDGAILKTNTNGTTVSGTNSEGAFSIHNHV ADNVLLENGGHLDINAYGS

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
210	949	1	296	FFSSIQLTDDQGPVLMTTVAMPVFSKQNETRSKGILLGVVGTD VPVKELLKTIPKYKVMNDLIPEIKATEMPRALFSQSSGFKLYF GAMFLLTTITAC
211	950	3	594	SCSGTGTNACYMEDMSNIDLVEGDEGRMCINTEWGAFGDDGAL EDIRTEFDRELDLGSLNPGKQLFEKMISGLYLGELVRLILLKM AKAGLLFGGEKSSALHTKGKIETRHVAAMEKYKEGLANTREIL VDLGLEPSEADCIAVQHVCTIVSFRSANLCAAALAAILTRLRE NKKVERLRTTVGMDGTLYKIHPQY
212	951	2	2167	FVAIATNGVVPAGGSYYMISRSLGPEFGGAVGLCFYLGTTFAG AMYILGTIEILLAYLFPAMAIFKAEDASGEAAAMLNNMRVYGT CVLTCMATVVFVGVKYVNKFALVFLGCVILSILAIYAGVIKSA FDPPNFPICLLGNRTLSRHGFDVCAKLAWEGNETVTTRLWGLF CSSRFLNATCDEYFTRNNVTEIQGIPGAASGLIKENLWSSYLT KGVIVERSGMTSVGLADGTPIDMDHPYVFSDMTSYFTLLVGIY FPSVTGIMAGSNRSGDLRDAQKSIPTGTILAIATTSAVYISSV VLFGACIEGVVLRDKFGEAVNGNLVVGTLAWPSPWVIVIGSFF STCGAGLQSLTGAPRLLQAISRDGIVPFLQVFGHGKANGEPTW ALLLTACICEIGILIASLDEVAPILSMFFLMCYMFVNLACAVQ TLLRTPNWRPRFRYYHWTLSFLGMSLCLALMFICSWYYALVAM LIAGLIYKYIEYRGAKKEWGDGIRGLSLSAARYALLRLEEGPP HTKNWRPQLLVLVRVDQDQNVVHPQLLSLTSQLKAGKGLTIVG SVLEGTFLENHPQAQRAEESIRRLMEAEKVKGFCQVVISSNLR DGVSHLIQSGGLGGLQHNTVLVGWPRNWRQKEDHQTWRNFIEL VRETTAGHLALLVTKNVSMFPGNPERFSEGSIDRWGIGHDGGM LMLVPFLLRHHKVWRKCKMRIFTVAQMVDMHAM
213	952	1	128	FYLRLLSFFCFQEHEKRCWSVDFNLMDPKLLASGSDDAKGTV
214	953	3	244	RNSKAMHRSSCDGPLLSLPSVGRSATHALVQAQLICSGARRGM HAFIVPIRSLQDHTPLPGKPIMLPQGTLPGGEPRWPP
215	954	2	609	CGTLILQARAYVGPHVLAVVTRTGFCTAKGGLVSSILHPRPIN FKFYKHSMKFVAALSVLALLGTIYSIFILYRNRVPLNEIVIRA LDLVTVVVPPALPAAMTVCTLYAQSRLRRQGIFCIHPLRINLG GKLQLVCFDKTGTLTEDGLDVMGVVPLKGQAFLPLVPEPRRLP VGPLLRALATCHALSRLQDTPVGDPMDLKM
216	955	292	855	QIEYFRSLLDEHHISYVIDEDVKSGRYMELEQRYMDLAENARF EREQLLGVQQHLSNTLKMAEQDNKEAQEMIGALKERSHHMERI IESEQKGKAALAATLEEYKATVASDQIEMNRLKAQLENEKQKV AELYSIHNSGDKSDIQDLLESVRLDKEKAETLASSLQEDLAHT RNDANRLQDAIAKGRG
217	956	2	400	ARYRFTLSARTQVGSGEAVTEESPAPPNEATPTAAPPTLPPTT VGATGAVSSTDATAIAATTEATTVPIIPTVAPTTMATTTTVAT TTTTTAAATTTTESPPTTTSGTKIHESAPDEQSIWNVTVLPNS KWA

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218	957	1	662	LKSTQDEINQARSKLSQLHESRQEAHRSLEQYDQVLDGAHGAS LTDLANLSEGVSLAERGSFGAMDDPFKNKALLFSNNTQELHPD PFQTEDPFKSDPFKGADPFKGDPFQNDPFAEQQTTSTDPFGGD PFKESDPFRGSATDDFFKKQTKNDPFTSDPFTKNPSLPSKLDP FESSDPFSSSSVSSKGSDPFGTLDPFGSGSFNSAEGFADFSTI EGRRG
219	958	1	752	RTRGGSGNSSQPSLREGHDKPVFNGAGKPHSSTSSPSVPKTSA SRTQKSAVEHKAKKSLSHPSHSRPGPMVTPHNKAKSPGVRQPG SSSSSAPGQPSTGVARPTVSSGPVPRRQNGSSSSGPERSISGS KKPTNDSNPSRRTVSGTCGPGQPASSSGGPGRPISGSVSSARP LGSSRGPGRPVSSPHELRRPVSGLGPPGRSVSGPGRSISGSIP AGRTVSNSVPGRPVSSLGPGQTVSSSGPTIKPKCT
220	959	439	582	RGKGITPRYHLCISDPHNLKICCRVNGEVVQSSNTNQMVFKTE DLIAW
221	960	230	420	VVAVTRWLCENGVSYLRKCVCSACRHGTRCAGEVAAAANNSHC TVGIAFNAKIGGMGNQLTWM
222	961	311	490	GAPPPFVPTLKSDDDTSNFDEPKKNSWVSSSPCQLSPSGFSGE ELPFVGFSYSKALGIL
223	962	2	422	FVERLAHLHAACAPRRKVALLLEVCRDVYAGLARGENQDPLGA DAFLPALTEELIWSPDIGDTQLDVEFLMELLDPDELRGEAGYY LTTWFGALHHIAHYQPETDRAPRGLSSEARASLHQWHRRRTLH RKDHPRAQQLD
224	963	385	844	FWMDPYNPLNFKAPFQTSGENEKGCRDSKTPSESIVAISECHT LLSCKVQLLGSQESECPDSVQRDVLSGGRHTHVKRKKVTFLEE VTEYYISGDEDRKGPWEEFARDGCRFQKRIQETEDAIGYCLTF EHRERMFNRLQGTCFKGLNVLKQC
225	964	3	166	AASTAYSFFGTVENMAPKVVNRPGHTQSADWGSFGGLMGRFEF GIFLKGKEIVK
226	965	1	118	GFVFLPGPMSVGLDFSLPGMEHVYGIPEHADNLRLKVTE
227	966	1	390	GSECQGTDLDTRNCTSDLCVHTASGPEDVALYVGLIAVAVCLV LLLLVLILVYCRKKEGLDSDVADSSILTSGFQPVSIKPSKADN PHLLTIQPDLSTTTTTYQGSLCPRQDGPSPKFQLTNGHLLSPL G
228	967	1	777	LIYNEDMICWIESRESSNQLKCIQITKAGGLTDEWTINILQSF HNVQQMAIDWLTRNLYFVDHVGDRIFVCNSNGSVCVTLIDLEL HNPKAIAVDPIAGKLFFTDYGNVAKVERCDMDGMNRTRIIDSK TEQPAALALDLVNKLVYWVDLYLDYVGVVDYQGKNRHAVIQGR QVRHLYGITVFEDYLYATNSDSYNIVRISRFNGTDIHSLIKIE NAWGIRIYQKRTQPTVRSHACEVDPYGMPGGCSHICLLSSSYT K
229	968	3	488	SSGNPQPGDSSGGGAGGGLPSPGEQELSRRLQRLYPAVNQQET PLPRSWSPKDKYNYIGLSQGNLRVHYKGHGKNHKDAASVRATH PIPAACGIYYFEVKIVSKGRDGYMGIGLSAQGVNMNRLPGWDK HSYGYHGDDGHSFCSSGTGQPYGPTFTTGDVI

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230	969	1	228	FFFFKMGSRSVTQAGVQWCDVSSLQAPPPRFTLFCLSLPSSWD YRCVPPCPANFFVFLVETGFHRVSQYGLDLLTS
231	970	2	119	QLSLARGKVFLCALSFVYFAKALAEGYLKSTITQIERRVDIPS SLVGVIDGSFEIGNLLVITFVSYFGAKLHRPKIIGAGCVIMGV GTLLIAMPQFFMEQYKYERYSPSSNSTLSISPCLLESSSQLPV SVMEKSKSKISNECEVDTSSSMWIYVFLGNLLRGIGETPIQPL GIAYLDDFASEDNAAFYIGCVQTVAIIGPIFGFLLGSLCAKLY VDIGFVNL/DHF*VSAQLGTRKGVLVCLVFCLLCQSIGRRLSE EHHHSDREKG
232	971	221	1068	QPAGRVEAFCKFHMWAEGMTSLMKAALDLTYPITSMFSGAGFN SSIFSVFKDQQIEDLWIPYFAITTDITASAMRVHTDGSLWRYV RASMSLSGYMPPLCDPKDGHLLMDGGYINNLPADVARSMGAKV VIAIDVGSRDETDLTNYGDALSGWWLLWKRWNPLATKVKVLNM AEIQTRLAYVCCVRQLEVVKSSDYCEYLRPPIDSYSTLDFGKF NEICEVGYQHGRTVFDIWGRSGVLEKMLRDQQGPSKKPASAVL TCPNASFTDLAEIVSRIEPAKPAM
233	972	133	635	LWVIMFVSYLILTLLHVQTAVLARPGGESIGCDDYLGSDKVVD KCGVCGGDNTGCQVVSGVFKHALTSLGYHRVVEIPEGATKINI TEMYKSNNYLALRSRSGRSIINGNWAIDRPGKYEGGGTMFTYK RPNEISSTAGESFLAEGPTNEILDVYVSLDVSGLFFGF
234	973	1	420	ISGGTRSAGPLRRNYNFIAAVVEKVAPSVVHVQLWGRNQQWIE VVLQNGARYEAVVKDIDLKLDLAVIKIESNAELPVLMLGRSSD LRAGEFVVALGSPFSLQNTATAGIVSTKQRGGKELGMKDSDMD YVQIDATINYG
235	974	2	860	PRVRELKEILDRKGHFSENETRWIIQSLASAIAYLHNNDIVHR DLKLENIMVKSSLIDDNNEINLNIKVTDFGLAVKKQSRSEAML QATCGTPIYMAPEVISAHDYSQQCDIWSIGVVMYMLLRGEPPF LASSEEKLFELIRKGELHFENAVWNSISDCAKSVLKQLMKVDP AHRITAKELLDNQWLTGNKLSSVRPTNVLEMMKEWKNNPESVE ENTTEEKNKPSTEEKLKSYQPWGNVPETNYTSDEEEEKQVGRI IAAFLPSVKYPHHTWNIFLQICLFVVSL
236	975	1	467	LSISVSDVSLSDEGQYTCSLFTMPVKTSKAYLTVLGVPEKPQI SGFSSPVMEGDLMQLTCKTSGSKPAADIRWFKNDKEIKDVKYL KEEDANRKTFTVSSTLDFRVDRSDDGVAVICRVDHESLNATPQ VAMQVLEMHYTPSVKIIPSTPFPQEG
237	976	3	417	YNQKVDLFSLGIIFFEMSYHPMVTASERIFVLNQLRDPTSPKF PEDFDDGEHAKQKSVISWLLNHDPAKRPTATELLKSELLPPPQ MEESELHEVLHHTLTNVDGKAYRTIDGPRSFRQRISPAIA\YT YD\SDILKGN

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238	977	2	740	DQDYKYDSTSDDSNFLNPPRGWDHTAPGHRTFETKDQPEYDST DGEGDWSLWSVCSVTCGNGNQKRTRSCGYACTATESRTCDRPN CPGIEDTFRTAATEVSLLAGSEEFNATKLFEVDTDSCERWMSC KSEFLKKYMHKVMNDLPSCPCSYPTEVAYSTADIFDRIKRKDF RWKDASGPKEKLEIYKPTARYCIRSMLSLESTTLAAQHCCYGD NMQLITRGKGAGTPNLISTEFSAELHYKVDV
239	978	2	612	ESEENGESAMDSTVAKEGTNVPLVAAGPCDDEGIVTSTGAKEE DEEGEDVVTSTGRGNEIGHASTCTGLGEESEGVLICESAEGDS QIGTVVEHVEAEAGAAIMNANENNVDSMSGTEKGSKDTDICSS AKGIVESSVTSAVSGKDEVTPVPGGCEGPMTSAASDQSDSQLE KVEDTTISTGLVGGSYDVLVSGEVPECEVAH
240	979	79	361	VCIICLIFSYYSFDSALQSAKSSLGGNDELSATFLEMKGHFYM YAGSLLLKMGQHGNNVQWRALSELAALCYLIAFQVSLPLGAID ISRSLDVF
241	980	2	681	QHPSQEKPQVLTPSPRKQKLNRKYRSHHDQMICKCLSLSISYS ATIGGLTTIIGTSTSLIFLEHFNNQYPASEVVNFGTWFLFSFP ISLIMLVVSWFWMHWLFLGCNFKETCSLSKKKKTKREQLSEKR IQEEYEKLGDISYPEMVTGFFFILMTVLWFTREPGFVPGWDSF FEKKGYRTDATVSVFLGFLLFLIPAKKPCFGKKNDGENQEHSL GTEPIITWKDF
242	981	1	491	LEREGDKGTPVLRGFSSVSGSWSRRMPPFLLLTCLFITGTSVS PVALDPCSAYISLNEPWRNTDHQLDESQGPPLCDNHVNGEWYH FTGMAGDAMPTFCIPENHCGTHAPVWLNGSHPLEGDGIVQRQA CASFNGNCCLWNTTVEVKACPGGYYVYRLTKPSV
243	982	1	983	CGRTMSDIRHSLLRRDALSAAKEVLYHLDIYFSSQLQSAPLPI VDKGPVELLEEFVFQVPKERSAQPKRLNSLQELQLLEIMCNYF QEQTKDSVRQIIFSSLFSPQGNKADDSRMSLLGKLVSMAVAVC RIPVLECAASWLQRTPVVYCVRLAKALVDDYCCLVPGSIQTLK QIFSASPRFCCQFITSVTALYDLSSDDLIPPMDLLEMIVTWIF EDPRLILITFLNTPIAANLPIGFLELTPLVGLIRWCVKAPLAY KRKKKPPLSNGHVSNKVTKDPGVGMDRDSHLLYSKLHLSVLQV LMTLQLHLTEKNLYGPPGADPLRPHG
244	983	32	362	SACSTGPELPGRATRSLTRPANQKGCDGDRLYYDGCAMIAMNG SVFAQGSQFSLDDVEVLTATLDLEDVRSYRAEISSRNLAVSAP VDTCVGCSSKTWKVAPFVRAWWRP
245	984	158	398	APLSRLCFPQVLVNEGGGFDRASGSFVAPVRGVYSFRFHVVKV YNRQTVQVTSALAPIPGSGGWGGGRRGAQLTSGWTLH
246	985	2	707	PHIIGAEDDDFGTEHEQINGQCSCFQSIELLKSRPAHLAVFLR HVVSQFDPATLLCYLYSDLYKHTNSKETRRIFLEFHQFFLDRS AHLKVSVPDEMSADLEKRRPELIPEDLHRHYIQTMQERVHPEV QRHLEDFRQKRSMGLTLAESELTKLDAERDKDRLTLEKERTCA EQIVAKIEEVLMTAQAVEEDKSSTMQYVILMYMKHLGVKVKEP RNLEHKRGRIGFLPKIKQSM

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247	986	18	441	SPGTGRGPGPTSFVCLPTPQCPFIDDFILALHRKIKNEPVVFP EGPEISEELKDLILKMLDKNPETRIGVPDIKLHPWVTKNGEEP LPSEEEHCSVVEVTEEEVKNSVRLIPSWTTVILVKSMLRKRSF GNPFEPQARMA
248	987	3	732	HASGIKIDKTSDGPKLFLTEEDQKKLHDFEEQCVEMYFNEKDD KFHSGSEERIRVTFERVEQMCIQIKEVGDRVNYIKRSLQSLDS QIGHLQDLSALTVDTLKTLTAQKASEASKVHNEITRELSISKH LAQNLIDDGPVRPSVWKKHGVVNTLSSSLPQGDLESNNPFHCN ILMKDDKDPQCNIFGQDLPAVPQRKEFNFPEAGSSSGALFPSA VSPPELRQRLHGVELLKIFNKKQKKRA
249	988	3	468	CCRWIDCFALYDQQEELVRHIEKVHIDQRKGEDFTCFWAGCPR RYKPFNARYKLLIHMRVHSGEKPNKCTFEGCEKAFSRLENLKI HLRSHTGEKPYLCQHPGCQKAFSNSSDRAKHQRTHLDTKPYAC QIPGCTKRYTDPSSLRKHVKAHSSK
250	989	356	553	LPLLWTLSDFGGTMDQSGMEIPVTLIIKAPNQKYSDQTISCFL NWTVGKLKTHLSNVYPSKPVSV
251	990	1	895	AGTRMCVVAAAEELVCGA\RGLWMRRTRRPRFVLMNKMDDLNL HYRFLNWRRRIREIREVRAFRYQERFKHILVDGDTLSYHGNSG EVGCYVASRPLTKDSNYFEVSIVDSGVRGTIAVGLVPQYYSLD HQPGWLPDSVAYHADDGKLYNGRAKGRQFGSKCNSGDRIGCGI EPVSFDVQTAQIFFTKNGKRVGSTIMPMSPDGLFPAVGMHSLG EEVRLHLNAELGREDDSVMMVDSYEDEWGRLHDVRVCGTLLEY LGKGKSIVDVGLAQARHPLSTRSHYFEVEIVDPGEKCYIA
252	991	51	674	QQAEEHLAAYSVSDSDSGKDPSMECCRRATPGTLLLFLAFLLL SSRTARSEEDRDGLWDAWGPWSECSRTCGGGASYSLRRCLSSK SCEGRNIRYRTCSNVDCPPEAGDFRAQQCSAHNDVKHHGQFYE WLPVSNDPDNPCSLKCQAKGTTLVVELAPKVLDGTRCYTESLD MCISGLCQVSADLFSFNLSRGFQCLCVNGLHSLTL
253	992	2	554	RLLRQELVVLCHLHHPSLISLLAAGIRPRMLVMELASKGSLDR LLQQDKASLTRTLQHRIALHVADGLRYLHSAMIIYRDLKPHNV LLFTLYPNAAIIAKIADYGIAQYCCRMGIKTSEGTPGFRAPEV ARGNVIYNQQADVYSFGLLLYDILTTGGRIVEGLKFPNEFDEL EIQGKLPDPVKE
254	993	3	437	KASNSTHEFRIGLPEGWESEKKAVIPLGIGPPLTLICLGVLGG ILIYGRKGFQTAHFYLKDSPSPKVISTPPPPIFPISKEVGPIP IKHFPKHVANLHASRGFTEKFETLKKFYQEGQSCTVDLGITAN SSNHPDNRHRNRSLI
255	994	3	445	SFPDRTASLVLLSVPVGQAGMQQRGLAIVALAVCAALHASPAI LPIASSCCTEVSHHISRRLLERVNMCRIQRADGDCDLAAVILH VKRRRICVSPHNHTVKQWMKVQAAKKNGKGNVCHRKKHHGKRN SNRAHQGKHETYGHKTPY

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256	995	2	737	FEQPGNPGDPRVRTPPPWGPHFFALIPSSPKEVPATPSSRRDP IAPTATLLSKKTPATLAPKEALIPPAMTVPSPKKTPAIPTPKE APATPSSKEASSPPAVTPSTYKGAPSPKELLIPPAVTSPSPKE APTPPAVTPPSPEKGPATPAPKGTPTSPPVTPSSLKDSPTSPA SVTCKMGATVPQASKGLPAKKGPTALKEVLVAPAPESTPIITA PTRKGPQTKKSSATSPPICPDPSAKNGSKG
257	996	79	3	FFLKIQGLGWARWLTPVIPVLWEAE
258	997	307	475	AGFGYGLPISRLYAKYFQGDLNLYSLSGYGTDAIIYLKVSLEF NSKILFLKPLLLL
259	998	26	622	WMRAPMLQKQQAPRMDTPPPEERLEKQNEKLNNQEEETEFKEL DGLREALANLRGLSEEERSEKAMLRSRIEEQSQLICILKRRSD EALERCQILELLNAELEEKMMQEAEKLKAQGEYSRKLEERFMT LAANHELMLRFKDEYKSENIKLREENEKLRLENNSLFSQALKD EEAKVLQLTVRCEALTGELETLKERC
260	999	2	241	DPGASHASVQVQVLKEQLFAGRMPSPFRSCALMGMCGSRSADN LSCPSPLNVMEPVSFFPLKSLGKGMIQHFRHIVSLV
261	1000	1	620	VTTTTHSVGRGHELQLLNEELRNIELECQNIMQAHRLQKVTDQ YGDIWTLHDGGFRNYNTSIDMQRGKLDDIMEHPEKSDKDSSSA YNTAESCRSTPLTVDRSPDSSLPRVINLTNKKNLRSTMAATQS SSGQSSKESTSTKAKTTEQGCSAESKEKVLEGSKLPDQEKAVS EHIPYLSPYHSSSYRYANIPAHARHYQSYMQLIQ
262	1001	3	420	VWGCLATVSTHKKIQGLPFGNCLPVSDGPFNNSTGIPFFYMTA KDPVVADLMKNPMASLMLPESEGEFCRKNIVDPEDPRCVQLTL TGQMIAVSPEEVEFAKQAMFSRHPGMRKWPRQYEWFFMKMRIE HIWLQKWYG
263	1002	43	441	QAANMAVARVDAALPPGEGSVVNWSGQGLQKLGPNLPCEADIH TLILDKNQIIKLENLEKCKRLIQLSVANNRLVRMMGVAKLTLL RVLNLPHNSIGCVEGLKELVHLEWLNLAGNNLIAMEQINSCTA LQHL
264	1003	3	834	FRAAVGAVPEGAWKDTAQLHKSEEAKRVLRYYLFQGQRYIWIE TQQAFYQVSLLDHGRSCDDVHRSRHGLSLQDQMERKAIYGPNV ISIPVKSYPQLLVDEAFSIALWLADHYYWYALCIFLISSISIC LSLYKTRKQSQTLRDMVKLSMRVCVCRPGGEEEWVDSSELVPG DCLVLSQEGGLMPCDAALVAGECMVNDSSLTGESIPVLKTALP EGLGPYCAETHRRHTLFCGTLILHARAYVGPHVLAVVTRTGMS REAGLERDPGSAPLKRWS
265	1004	2	670	FVGGGLHLHLCLLLCFMLPEDAAMAVLTASNHVSNVTVNYNIT VERMNRMQGLRVSTVPAVLSPNATLALTAGVLVDSAVEVAFLW TFGDGEQALHQFQPPYNESFPVPDPSVAQVLVEHNVTHTYAAP GEYVLTVLASNAFENRTQQVLIRSGRVPIVSLECVSCKAQAVY EVSRSSYVYLEGRCLNCSSGSKRGRWAARTFSNKTLVLDETTT STGSASM

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266	1005	2	1093	PEFLGRLFRGKAATLHVHSDQKPLHDGALGSQQNLVRMKEALR ASTMDVTVVLPSGLEKRSVLNGSHAMMDLLVELCLQNHLNPSH HALEIRSSETQQPLSFKPNTLIGTLNVHTVFLKEKVPEEKVKP GPPKVPEKSVRLVVNYLRTQKAVVRVSPEVPLQNILPVICAKC EVSPEHVVLLRDNIAGEELELSKSLNELGIKELYAWDNRRETF RKSSLGNDETDKEKKKFLGFFKVNKRSNSKGCLTTPNSPSMHS RSLTLGPSLSLGSISGVSVKSEMKKRRAPPPPGSGPPVQDKAS EKVSLGSQIDLQKKKRRAPAPPPPQPPPPSPLIPNRTEDKEEN RKSTMVYCCASFPTQAKRF
267	1006	686	400	VQWHNLHSLQPLPAGFK*FLCFSLPSSWDYRCAPPLP/APFFF YFLFLVELGFHHIG*AGLELTSTDLPASAS/ESAGITGMSHRA RPMDFFLLKIL
268	1007	1	453	GRRFRPPSDEEREPWEPWTQLRLSGHLKPLHYNLMLTAFMENF TFSGEVNVEIACRNATRYVVLHASRVAVEKVQLAEDRAFGAVP VAGFFLYPQTQVLVVVLNRTLDAQRNYNLKIIYNALIENELLG FFRSSYVLHGERRFLGVTQFSP
269	1008	333	526	KELDPFYNS*RKIKYLRIYLTKEVKDLYKENYKTLLKEITDDT N/KKHIPSSWTGRINTVKMTIL
270	1009	699	882	VPHPLQAIHEQMNCKEYQEDLALRAQNDAAARRPSEMFKVRLA QGRGLASLSSGIQSGVG
271	1010	16	148	RWNSLTCVVLTFLGHRLLKRFLVPKLRRFLKPQGHPRLLLWFK R
272	1011	1	659	YGEFVTYQGVAVTRSRKEGIAHNYKNETEWRANIDTVMAWFTE EDLDLVTLYFGEPDSTGHRYGPESPERREMVRQVDRTVGYLRE SIARNHLTDRLNLIITSDHGMTTVDKRAGDLVEFHKFPNFTFR DIEFELLDYGPNGMLLPKEGRLEKVYDALKDAHPKLHVYKKEA FPEAFHYANNPRVTPLLMYSDLGYVIHGVSRLLEAPPPGAPSP GSGS
273	1012	146	413	RIPLLRLRSSTYRSKGFDVTVKHSHGSWTGFGGEDLATIPKGL NTYFLVNIATIFESKNFFLPGIKWNGILGLSYATLAKPSSSLE TFF
274	1013	3	251	IKSYSGPNGRSCQIWQRLRWGSRELLLGWKLSHSFSTCPFQFP DIVEFCEAMANAGKTVIVAALDGTFQRKVRRLIQVWSWD
275	1014	326	651	YCFCFDLLH*CIHRDVKPENILITKHSVIKLCDFGFARLLTGP SDYYTDYVATRWYRSPELPVGDTQY\GPPV\DVW\AIGCVSAE \LLSGKCLWWPGKS/DMLDQLYLIRK
276	1015	224	435	RGWALDWIGADLSLHLQEEVETEVAWEECGHVLLSLCYSSQQG GLLVGVLRCAHLAPMDANGYSDPFVRL
277	1016	2	429	GGILAMEYAPGGTLAEFIQKRCNSLLEEETILHFFVQILLALH HVHTHLILHRDLKTQNILLDKHRMVVKIGDFGISKILSSKSKA YTVVGTPCYISPELCEGKPYNQKSDIWALGCVLYELASLKRAF EAANLPALVLKIM

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278	1017	1	262	VQCGGIHQVSGAVVVSGLLQGMMGLLGSPGHVFPHCGPLVLAP SLVVAGLSAHREVAQFCFTHWGLALLYVSPERRGMVPSGGVWG D
279	1018	1	480	PRMTGSTHASAPSYGGSCRNNLFYREETYTPKAETDEMNEVET APIPEENHVWLQPRVMRPTKPKKTSAVNYMTQVVRCDTKMKDR CIGSTCNRYQCPAGCLNHKAKIFGSLFYESFASICRAAIHYGI LDDKGGLVDITRNGKVPFFVKSERHGVQSLR
280	1019	271	792	VPQNIICAFFCVPCRFASTIPFWGLTLHLQHLGNNVFLLQTLF GAVTLLANCVAPWALNHMSRRLSQMLLMFLLATCLLAIIFVPQ EMQTLRVVLATLGVGAASLGITCSTAQENELIPSIIRGRATGI TGNFANIGGALASLVMILSIYSRPLPWIIYGVFAILSGLVVLL LP
281	1020	2	679	VLVSRDHMKSAQQFFQLVGGSASECDTIPGRQCMASCFFLLKQ FDDVLIYLNSFKSHFYNDDIFNFNYAQAKAATGNTSEGEEAFL LIQSEKMKNDYIYLSWLARGYIMNKKPRLAWELYLKMETSGES FSLLQLIANDCYKMGQFYYSAKAFDVLERLDPNPEYWEGKRGA CVGIFQMIIAGREPKETLREVLHLLRSTGNTQVEYMIRIMKKW AKENRVSILK
282	1021	3	359	LKVSDELVQQYQIKNQCLSAIASDAEQEPKIDPYAFVEGDEEF LFPDKKDRQNSEREAGKKHKVREITVHQRVTVDFVALHIVTLL LPQLSHFFCLRIERVIIYLEKPIFARLRWLMP
283	1022	3	538	GVPRNLPSSLEYLLLSYNRIVKLAPEDLANLTALRVLDVGGNC RRCDHAPNPCMECPRHFPQLHPDTFSHLSRLEGLVLKDSSLSW LNASWFRGLGNLRVLDLSENFLYKCITKTKAFQGLTQLRKLNL SFNYQKRVSFAHLVSGPPFLRGSLGRPLKGAGTWHGNLSFPLH FEWGKT
284	1023	3	442	ILFAALIWSSFDENIEASAGGGGGSSIDAVMVDSGAVVEQYKR MQSQESSAKRSDEQRKMKEQQAAEELREKQAAEQERLKQLEKE RLAAQEQKKQAEEAAKQAELKQKQAEEAAAKAAADAKAKAEAD AKAAEEAAKKAAADAKK
285	1024	1	119	AMEIVHEPRDLERYMREAVKVSNDSPVLLDRFLNDAIEC
286	1025	67	227	MLSPGYDYGYVCVEFSLLEDAIGCMEANQVALYFGQMMLEGYI FLYMGREGFK
287	1026	2	1101	PRVRSSGGQEDPASQQWARPRFTQPSKMRRRVIARPVGSSVRL KCVASGHPRPDITWMKDDQALTRPEAAEPRKKKWTLSLKNLRP EDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVLTGTHPVNT TVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVG GQKFVVLPTGDVWSRPDGSYLNKLLITRARQDDAGMYICLGAN TMGYSFRSAFLTVLPDPKPPGPPVASSSSATSLPWPVVIGIPA GAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSG DKDLPSLAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLY PKLYT\DIPHHTHTHTPHPPAN
288	1027	3	96	NFHFTGKCLFMSGLSEVQLTHMDDHTLPGY

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289	1028	95	407	SPRKRKTRHSTNPPLECHVGWVMDSRDHGPGTSSVSTSNASPS EGAPLAGSYGCTPHSFPKFQHPSHELLKENGFTQQVYHKYRRR CLSERKRLGIGQSQEMNT
290	1029	1	359	PGSGGSAGGRDGSAYQGALLPREQFAAPLGRPVGTSYSATYPA YVSPDVAQSWTAGPFDGSVLHGLPGRRPTFVSDFLEEFPGEGR ECVNCGALSTPLWRRDGTGHYLCNACGLYHKMN
291	1030	2	513	PDHRHGALWWWYSCGVLPVTVSRNEGDERNQVLTLYLWIRQEW TDAYLRWDPNAYGGLDAIRIPSSLVWRPDIVLYNKYCLS/AAP PLSYPSLDLPLAVGV**SPLPTT*PGCHAALEAFPQDPSKLPS TQPLHGTPTLGYPRPAQAERLLGTYCVVQGRCLNHKGLSRAHF
292	1031	1	595	YALTGALVIVTGMVMGNIADYFNLPVSSMSNTFTFLNAGILIS IFLNAWLMEIVPLKTQLRFGFLLMVLAVAGLMFSHSLALFSAA MFILGVVSGITMSIGTFLVTQMYEGRQRGSRLLFTDSFFSMAG MIFPMIAAFLLARSIEWYWVYACIGLVYVAIFILTFGCEFPAL CSHATKLGTASSYPSLDVVQLRTLNA
293	1032	71	479	MAKVGLKTEHYDRYPHMFSGGQRQRIAIARGLMLDPDVVIADE PVSALDVSVRAQVLNLMMDLQQELGLSYVFISHDLSVVEHIAD EVMVMYLGRCVEKGTKDQIFNNPRHPYTQALLSATPRLNPDDR RERIKLSX*
294	1033	2	427	SATLERVLNHPDETQARRLMTLEDIVSGYSNVLISLADSQGKT VYHSPGAPDIREFTRDAIPDKDAQGGEVYLLSGPTMMMPGHGH GHMEHSNWRMINLPVGPLVDGKPIYTLYIALSIDFHLHYINDL MNKLIMTASVII
295	1034	3	342	VLAYPGIKVSTAEARAILPAQYRRQDCIAHGRHLAGFIHACYS RQPELAAKLMKDVIAEPYRERLLPGFRQARQAVAEIGAVASGI SGSGPTLFALCDKPETAQRVADWLGK
296	1035	2	279	GQQQRVALARALILKPKVLLFDEPLSNLDANLRRSMRDKIREL QKQFDITSLYVTHDQSEAFAVSDTVLVMNKGHIMQIGSPQDLR VRRLNW
297	1036	3	157	AVHYLERVRIAEHAHKFPGQISGGQQQRVAIARSLCMKPKIML FDEPTSAL
298	1037	1	217	APYDAENYFDYDNLNNGPSLQHWFGVDSLGRDIFSRVLVGAQI SLAAGVFAVFIGAAIGTLLGLLAGYYEGW
299	1038	3	570	VFCLIADLDPIDELVDFPIVYASALNGIAGLDHEDMAEDMTPL YQAIVDHVPAPDVDLDGPFQMQISQLDYNSYVGVIGIGRIKRG KVKPNQQVTIIDSEGKTRNAKVGKVLGHLGLERIETDLAEAGD IVAITGLGELNISDTVCDTQNVEALPALSVDEPTVSMFFCVNT SPFCGKEGKFVTSRQI
300	1039	1	366	QGTRAESQGSSKDKTRLAFAGLKFGDYGSIDYGRNYGVAYDIG AWTDVLPEFGGDTWTQTDVFMTQRATGVATYRNNDFFGLVDGL NFAAQYQGKNDRSDFDNYTEGNGHGFGFSATYEYEG
301	1040	3	201	DTYSVSIPLGATINMAGAAITITVLTLAAVNTLGIPVDLPTAL LLSVVASLCACGASGVAGGSLL

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302	1041	1	140	ANAQQGLPSGITLKLNNLVDKGLVDRLYAASSSGVPVNLLVRG TCS
303	1042	2	442	ARMTLIPGTHLLENIHNIWVNGVGTNSAPFWRMLLNSFVMAFS ITLGKITVSMLSAFAIVWFRFPLRNLFFWMIFITLMLPVEVRI FPTVEVIANLQMLDSYAGLTLPLMASATATFLFRKLNMSGPDK VVPAARISGYGPRVRKQ
304	1043	2	403	CAKCLRDADECPSGAFERIGRDISLDALEREVMKDDIFFRTSG GGVTLSGGEVLMQAEFATRFLQRLRLWGVSCAIETAGDAPASK LLPLAKLCDEVLFDLKIMDATQARDVVKMNLPRVLENLRLLVS EGVN
305	1044	1	346	YLLLFVCFLVMSLLVGLVYKFTAERAGKQSLDDLMNSSLYLMR SELREIPPHDWGKTLKEMDLNLSFDLRVEPLSKYHLDDISMHR LRGGEIVALDDQYTFLQRIPRSHYVLAVG
306	1045	1	207	VELFLSDEGDDVVIEVADQGCGVPESLRDKIFEQGVSTRADEP GEHGIGLYLIASYVTRCGGVITLEDN
307	1046	3	213	DAIIAPDANALPAAAQAAENLKNDKVAIVGFSTPNVMRPYVER GTVKEFGLWDVVQQGKISVYVADALQ
308	1047	1	129	YIVVTGKTHCGTPLTTVTGDATQSGYLTLNLPEMWEVSGYNRV
309	1048	271	46	XEGVEPDINASKTRQQLNDVAGKMKIIEARLSALTNNQTKSLK LNPVALPKVASQLLDELGYSLLARRADLQSAHX*
310	1049	16	253	ENIAEEYATKRYRSNVINWGMLPLQMAEVPTFEVGDYIYIPGI KAALDNPGTTFKGYVIHEDAPVTEITLYMESQEART
311	1050	2	299	LQTEIGSMVYAVKPGDGSAREQAASCQRVIGGLANIAEEYATK RYRSNVINWGMLPLQMAEVPTFEVGDYIYILGFKAAKYSPGTA FTVYAISGYGPRI
312	1051	1	344	TLEDLLMALDGEQHLQQQVSEKVLADNVLIAPGSVKPDATFWS ALIQDRYNVMTCIEKDACVLVEQDLNSDGQAERILFAFNDDRV IVYGFDSDRKEWDALDMSLLPNEITKEK
313	1052	2	630	ESNSRCRKMPGERCRGGPARLSLLLDLPTRPLPHPRQVIDFGS ASIFSEVRYVKEPYIQSRFYRAPEILLGLPFCEKVDVWSLGCV MDELHLGWPLYPGNNEYDQVRYICETQGLPKPHLLHAACKAHH FFKRNPHPDAANPWQLKSSADYLAETKVRPLERRKYMLKSLDQ IETVNGGSVASRLTFPDREALAEHADLKSMVEL/MKRLL
314	1053	1	302	RLVKKRVECRQCGKAGRNQSTLKTHMRSHTGEKPYECDHCGKA FSIGSNLNVHRRIHTGEKPYECLVCGEAFSDHSSLRSHVKTHR GEKLFVSSVWKRLQ
315	1054	1318	730	CGPGFSLSFFFLRWSF\ALVAQAGVQWHDLGSLQPPAPGFKRF SSLSLLSRWDYRHAHARLIFVFLVEMGFLHVGQAGLELPTSGD PPTSASQSARITGVTTPLGTFFFFLRWSFALVAQAGGQCLDLG SLQLPPPGFKRLVCHFQTPQKHRCSCQAPGDCLQESFVMTGCV LRTVSESVQRANAGAGAETVQGL

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316	1055	2486	1429	MGNAAAAKKGSEQESVKEFLAKAKEDFLKKWESPAQNTAHLDQ FERIKTLGTGSFGRVMLVKHKETGNHYAMKILD*QKVGKLKQI EHTLNEKRILQAVNFPFLVKLEFSFKDNSNLYMVMEYVPGGEM FSHLRRIGRFSEPHARFYAAQIVLTFEYLHSLDLIYRDLKPEN LLIDQQGYIQVTDFGFAKRVKGRTWTLCGTPEYLAPEIILSKG YNKAVDWWALGVLIYEMAAGYPPFFADQPIQIYEKIVSGKVRF PSHFSSDLKDLLRNLLQVDLTKRFGNLKNGVNDIKNHKWFATT DWIAIYQRKVEAPFIPKFKGPGDTS\NFDDYEEEEIRV\SINE KFG\KEFSEF
317	1056	867	461	SSSRSSHGDSPPHSQTPCDTNRGLDTKH*/DSQSIEEKDSSQS E*NRIERRKEVERILQTNSDYM*HWSN*PENILPKKFFSKHQK CTATLSMRNTSIM/KKEGLF*AQFPSLLLSHLPAVGLGIYTGT HLTTSTSTF
318	1057	544	784	TFHSSLEKNILQPCR*RRA\ICLPLLL*PSVPLLAPQYFSDLR NSIVNSQPPEKQQAMHLCFENLMEGIERNLLTKNRDR
319	1058	1606	228	GTSGVQQEISRLTNENLDLKELVEKLEKNERKLKKQLKIYMKK AQDLEAAQALAQSERKRHELNRQVTVQRKEKDFQGMLEYHKED EALLIRNLVTDLKPQMLSGTVPCLPAYILYMCIRHA\DYTNDD LKVHSLLTSTINGIKKVLKKHNDDFEMTSFWLSNTC\RLLHCL KQYSGDEGFMTQNTAKQN\EHCLKNFDLTEYRQV\L\SDLSIQ IYQQLIKIAEGVLQPMIVSAMLEN*SIQGLSGVKPTGSQKHSS SMADEDNSYRLEAIIRQMNAFHTVMCDQGLDPEIILQVFKQLF YMINAVTLNDLLLRKDVCSWSTGMQLRYNISQLEEWLRGRNLH QSGAVQTMEPLIQAAQLLQLKKKTQEDAEAICSLCTSLSTQQI VKILNLYTPLNEFEERVTVAFIRTIQAQLQERNDPQQLLLDAK HMFPVLFPFNPSSLTMDSIHIPACLNLEFLNEV
320	1059	3	250	HEENTILKAAEVQVPPK*VVTPEAKAFI*RCLAYQKEDCIDAQ QLACDP\YLLHYIQKLVFVSSPAGAAIASTFGVSNSCSSN
321	1060	1332	500	GTTDEIMTRWARVSTTYNKRPLPATSWEDMKKGSFEGTSQNLP KRKQLEANRLSLKNDAPQAKHKKNKKKKEYLNEDVNGFMEYLR QNSQMVHNGQIIATDSEEVREEIAVALKKDSRREGRRLKRQAA KKNAMVCFHCRKPGHGIADCPAALENQDMGTGICYRCGSTEHE ITKCKAKVDPALGEFPFAKCFVCGEMGHLSRSCPDNPKGLYAD GGGCKLCGSVEHLKKDCPESQNSERMVTVGRWAKGMSADYEEI LDVPKPQKPKTKIPKVVNF
322	1061	384	102	DHVRKSLLKNRAENIVNIFKCNVVSLPNLPAFGQAQWLTPVIP ALWEAEVGGS*GQEIETILANAVK/SPFLLKIQKKKISRAWWR AP/VSPRYSGG

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323	1062	1	777	SDAWADAWARSLSVSPSSYPELHTEVPLSVLILGLLVVFILSV CFGAGLFVFVLKRRKGVPSVPRNTNNLDVSSFQLQYGSYNTET HDKTDGHVYNYIPPPVVQMCQNPIYMAGREGRPSSLLPKPGKE FQLLGNLEEKKEEPATPAYTISATELLEKQATPREPELLYQNI AE/PSQGTS/TAQA*STITFVPYLKGQFAPSYESRRQNQDRIN KTVLYGTPRKCFVGQSKPNHPLLQAKPQSEPDYLEVLEKQTAI SQL
324	1063	1	1496	ALCHIAVGQQMNLHWLHKIGLVVILASTVVAMSAVAQLWEDEW EVLLISLQGTAPFLHVGAVAAVTMLSWIVAGQFARAERTSSQV TILCTFFTVVFALYLAPLTISSPCIMEKKDLGPKPALIGHRGA PMLAPEHTLMSFRKALEQKLYGLQADITISLDGVPFLMHDTTL RRTTNVEEEFPELARRPASMLNWTTLQRLNAGQWFLKTDPFWT ASSLSPSDHREAQNQSICSLAELLELAKGNATLLLNLRDPPRE HPYRSSFINVTLEAVLHSGFPQHQVMWLPSRQRPLVRKVAPGF QQTSGSKEAVASLRRGHIQRLNLRYTQVSRQELRDYASWNLSV NLYTVNAPWLFSLLWCAGVPSVTSDNSHTLSQVPSPLWIMPPD EYCLMWVTADLVSFTLIVGIFVLQKWRLGGIRSYNPEQIMLSA AVRRTSRDVSIMKEKLIFSEISDGVEVSDVLSVCSDNSYDTYA NSTATPVGPRGGGSHTKTLIERSGR
325	1064	1899	776	NSADYGDGPDSSDADPDSGTEEGVLDFSDPFSTEVKPRILLMG LRRSGKSSIQKVVFHKMSPNETLFLESTNKICREDVSNSSFVN FQIWDFPGQIDFFDPTFDYEMIFRGTGALIFVIDSQDDYMEAL ARLHLTVTRAYKVNTDINFEVFIHKVDGLSDDHKIETQRDIHQ RANDDLADAGLEKIHLSFYLTSIYDHSIFEAFSKVVQKLIPQL PTLENLLNIFISNSGIEKAFLFDVVSKIYIATDSTPVDMQTYE LCCDMIDVVIDISCIYGLKEDGAGTPYDKESTAIIKLNNTTVL YLKEVTKFLALVCFVREESFERKGLIDYNFHCFRKAIHEVFEV RMKVVKSRKVQNRLQKKKRATPNGTPRVLL
326	1065	1181	346	RTRGRDPGAGFRRTANKRCCRRRFLIGCGWLPLRSDWPLVSKM LSKGLKRKREEEEEKEPLAVDSWWLDPGHAAVAQAPPAVASSS LFDLSVLKLHHSLQQSEPDLRHLVLVVNTLRRIQASMAPAAAL PPVPSPPAAPSVADNLLASSDAALSASMASLLEDLSHIEGLSQ APQPLADEGPPGRSIGGAAPSLGALDLLGPATGCLLDDGLEGL FEDIDTSMYDNELWAPASEGLKPGPEDGPGKEEAPELDEAELD YLMDVLVGTQALERPPGPGR

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
327	1066	1844	337	LQEVKARRNTLHKEKDHLVNDYEQNMKLLQTKYDADINLLKQE HALSASKASSMIEELEQNVCQLKQQLQESELQRKQQLRDQENK FQMEKSHLKHIYEKKAHDLQSELDKGKEDTQKKIHKFEEALKW KKWRQI*LDPN/LLREKQSKEFLWQLEDIRQRYEQQIVELKLE HEQEKTHLLQQHNAEKDSLVRDHEREIENLEKQLRAANMEHEN QIQEFKKRDAQVIADMEAQVHKLREELINVNSQRKQQLVELGL LREEEKQRATREHEIVVNKLKAESEKMKIELKKTHAAETEMTL EKANSKLKQIEKEYTQKLAKSSQIIAELQTTISSLKEENSQQQ LAAERRLQDVRQKFEDEKKQLIRDNDQAIKVLQDELENRSNQV RCAEKKLQHKELESQEQITYIRQEYETKLKGLMPASLRQELED TISSLKSQVNFLQKRASILQEE/RDYISRQKVQPISR*LHERM QRMRISRLCCGTSSSRFEDLDIVNCEISGIF
328	1067	1149	238	VINLVYLISSPRPELKPVDKESEVVMKFPDGFEKFSPPILQLD EVDFYYDPKHVIFSRLSVSADLESRICVVGENGAGKSTMLKLL LGDLAPVRGIRHAHRNLKIGYFSQHHV\EQL\DLNVQCLWELA GHASFPG\RPEEEY\RHQLGFGMGISGEL\AMRPLCQPVLGAR KKPKWPFAQMDYCPAPTFYIL\DEPTN\HLGHGRAIEALGPCL QTISGVGVILVSHE*SALSRLVCRE\LWVC*G\GGVTRVERKD FDQYRALLQGTVSAREGFPLGPPRLKDSPRDMGLVSQTPWGHH VGYPLPGRG
329	1068	26	674	CSAVEVKMAARTAFGAVCRRLWQGLGNFSVNTSKGNTAKNGGL LLSTNMKWVQFSNLHVDVPKDLTKPVVTISDEPDILYKRLSVL VKGHDKAVLDSYEYFAVLAAKELGISIKVHEPPRKIERFTLLQ SVHIYKKHRVQYEMRTLYRCLELEHLTGSTADVYLEYIQRNLP EGVAMEVTKFCFFIFL\TQLEQLPEHIKEPIWETLSEEKEESK S
330	1069	2105	1283	DFWDTAGQERFQSMHASYYHKTHACIMVFDVQRKVTHRNLSTW YTELREFRPEIPCIVVANKIDGGAIPAPGC*QFTGDLPSYISS SIPRAGNLQ*LVLPPTIRYNPWLVACILPTL*RSQLSRPALFP RHRSLLTELFLGPVSQSSLPIPLSGMKASSGPPLQTFFPSLDR QTNVLPSLY\ADINVTQKSFNFAKKFSLPLYFVSAADGTNVVK LFNDAIRLAVSYKQNSQDFMDEIFQELENFSLEQEEEDVPDQE QSSSIETPSEEVASPHS
331	1070	1	1109	GATPLGSVGGRTGKMDAATLTYDTLRFAEFEDFPETSEPVWIL GRKYSIFTEKDEILSDVASRLWFTYRKNFPAIGGTGPTSDTGW GCMLRCGQMIFAQALVCRHLGRDWRWTQRKRQPDSYFSVLNAF IDRKDSYYSIHQIAQMGVGEGKSIGQWYGPNTVAQVLKKLAVF DTWSSLAVHIAMDNTVVMEEIRRLCRTSVPCAGATAFPADSDR HCNGFPAGAEVTNRPSPWRPLVLLIPLRLGLTDINEAYVETLK HCFM\MPQSLGVIGGKPNSAH\YFIG*VG\EELIYLDPHTTQP AVEPTDGCFIPDESFHCQHPPCRMSIAELDPSIAVVRGGHLST QAFGAECCLGMTRKTFGFLRFFFSMLG
332	1071	39	284	ALCVVPFNTFHN\DFLLLDKEGTLDPVMDSFSTHWTTIGPADM FFS\FRQHYKNFKSHGTNPSKSVWAHATCQSCAFPNLLGW

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333	1072	2	1484	TRLAEFGTRDPCAQAPCEQQCEPGGPQGYSCHCRLGFRPAEDD PHRCVDTDECQIAGVCQQMCVNYVGGFECYCSEGHELEADGIS CSPAGAMGAQASQDLGDELLDDGEDEEDEDEAWKAFNGGWTEM PGILWMEPTQPPDFALAYRPSFPEDREPQIPYPEPTWPPPLSA PRVPYHSSVLSVTRPVVVSATHPTLPSAHQPPVIPATHPALSR DHQIPVIAANYPDLPSAYQPGILSVSHSAQPPAHQPPMISTKY PELFPAHQSPMFPDTRVAGTQTTTHLPGIPPNHAPLVTTLGAQ LPPQAPDALVLRTQATQLPIIPTAQPSLTTTSRSPVSPAHQIS VPAATQPAALPTLLPSQSPTNQTSPISPTHPHSKAPQIPREDG PSPKLALWLPSPAPTAAPTALGEAGLAEHSQRDDRWLLVALLV PTCVFLVVLLALGIVYCTRCGPHAPNKRITDCYRWVIHAGSKS PTEPMPPRGSLTGVQTCRTSV
334	1073	1	1406	LRVRRRPHLPAPPALRARRSDRRSSRAPAAFPPRPPHASPAPG PAMAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPA TTGAVVTISASLVAKDNGSLALPADAHLYRFHWIHTPLVLTGK MEKGLSSTIRVVGHVPGEFPVSVWVTAADCWMCQPVARGFVVL PITEFLVGDLVVTQNTSLPWPSSYLTKTVLKVSFLLHDPSNFL KTALFLYSWDFGDGTQMVTEDSVVYYNYSIIGTFTVKLKVVAE WEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVLGPTLIQTF QKMTVTLNFLGSPPLTVCWRLKPECLPLEEGECHPVSVASTAY NLTHTFRDPGDYCFSIRAENIISKTHQYHKIQVWPSRIQPAVF AFPCATLITVMLAFIMYMTLRNATQQKDMVENPEPPSGVRCCC QMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV
335	1074	1	866	VVEFAFQLSSVSVCLTVSFGWQLGTVSSCLSRDWFLKGNLLII IVSVLIILPLALMKHLGYLGYTSGLSLTCMLFFLVSVIYKKFQ LGCAIGHNETAMESEALVGLPSQGLNSSCEAQMFTVDSQMSYT VPIMAFAFVCHPEVLPIYTELCRPSKRRMQAVANVSIGAMFCM YGLTATFGYLTFYSSVKAEMLHMYSQKDPLILCVRLAVLLA\V TLTVPVVLFPIRRALQQLLFPGKAFSWPRHVAIALILLVLVNV LVICVPTIRDIFGVIGSTSAPSLIFILPSCI
336	1075	3	825	GAGSKSSMMQLMHLESFYEK\PPPGLIKEDDTKPEDCIPDVPG NEHAREFLAHTPTKGLWMPLEKEVKVKH/CTFHWIAS*FLGDG KFIPKATRLKDVWVSN*FTCLFWDLTRFIHDCIFF*NWSLMNK NFNIIY*FFISLR*NTLILQKYFPFSLLLGWHCKWYGHRTGYK ECPFFIKDNQKLQQFRVAHEDFMYDIIRDNKQHEKNVRIQQLK QLLEDSTSGEDRSSSSSSEGKEKHKKKKKKEKHKKRKKEKKKK KKRKHKSSKSNEGSDSE

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337	1076	3	2451	EIAGAAAENMLGSLLCLPGSGSVLLDPCTGSTISETTSEAWSV EVLPSDSEAPDLKQEERLQELESCSGLGSTSDDTDVREVSSRP STPGLSVVSGISATSEDIPNKIEDLRSECSSDFGGKDSVTSPD MDEITHDFLYILQPKQHFQHIEAEADMRIQLSSSAHQLTSPPS QSESLLAMFDPLSSHEGASAVVRPKVHYARPSHPPPDPPILEG AVGGNEARLPNFGSPMF*LPAEMEAFKQRHS/YTPERLVRSRS S\DIVSSVRRPMSDPSWNRRP\GNEERELPPAAAIGATSLVAA PHSSSSSPSKDSSRGETEERKDSDDEKSDRNRPWWRKRFVSAM PKAPIPFRKKEKQEKDKDDLGPDRFSTLTDDPSPRLSAQAQVA EDILDKYRNAIKRTSPSDGAMANYESTEVMGDGESAHDSPRDE ALQNISADDLPDSASQAAHPQDSAFSYRDAKKKLRLALCSADS VAFPVLT\HSTRNGLPDHTDPEDNEIVCFLKVQIAEAINLQDK NLMAQLQETMRCVCRFDNRTCRKLLASIAEDYRKRAPYIAYLT RCRQGLQTTQAHLERLLQRVLRDKEVANRYFTTVCVRLLLESK EKKIREFIQDFQKLTAADDKTAQVEDFLQFLYGAMAQDVIWQN ASEEQLQDAQLAIERSVMNRIFKLAFYPNQDGDILRDQVLHEH IQRLSKVVTANHRALQIPEVYLREAPWPSAQSEIRTISAYKTP RDKVQCILRMCSTIMNLLSLANEDSVPGADDFVPVLVFVLIKA NPPCLLSTVQYISSFYASCLSGEESYWWMQFTAAVEFIKTIDD RK
338	1077	536	1305	WPMSLARGHGDTAASTAAPLSEEGEVTSGLQALAVEDTGGPSA SAGKAEDEGEGGREETEREGSGGEEAQGEVPSAGGEEPAEEDS EDWCVPCSDEEVELPADGQPWMPPPSEIQRLYELLAAHGTLEL QAEILPRRPPTPEAQSEEERSDEEPEAKEEEEEKPHMPTEFDF DDEPVTPKDSLIDRRRTPGSSARSQKREARLDKVLSDMKRHKK LEEQILRTGRDLFSLDSEDPSPASPPLRSSGSSLFPRQRKY
339	1078	2	1771	LGRGTFGQVV*CWKRGTNEIVAIKILKNHPSYARQGQIEVSIL ARLSTESADDYNFVRAYECFQHKNHTCLVFEMLEQNLYDFLKQ NKFSPLPLKYIRPVLQQVATALMKLKSLGLIHADLKPENIMLV DPSRQPYRVKVIDFGSASHVSKAVCSTYLQSRYYRAPEIILGL PFCEAIDMWSLGCVIAELFLGWPLYPGASEYDQI/RYISQTQG LPAEYLLSAGTKTTRFFNRDTDSPYPLWRLKTPDDHEAETGIK SKEARKYIFNCLDDMAQVNMTTDLEGSDMLVEKAVRREFIDLL KKMLSIDSVKRFSPVGSLNHPFVTMSLFLDFPHSTHVKSCFQN MEICKRRVNMYDTVNQSKTPFITHVAPSTSTNLTMTFNNQLTT VHNQPSAASMAAVAQRSMPLQTGTAQICARPDPFQQALIVCPP GFQGLQASPSKHAGYSVRMENAVPIVTQAPGAQPLQIQPGLLA QQAWPSGTQQILLPPAWQQLTGVATHTSVQHAAVIPETMAGTQ QLADWRNTHAHGSHYNPIMQQPALLTGHVTLPAAQPLNVGVAH VMRQQPTSTTSSRKSKQHLYCGRARVSKIASR

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340	1079	2	2721	EFAICRYPLGMSGGQIPDEDITASSQWSESTAAKYGRLDSEEG DGAWCPEIPVEPDDLKEFLQIDLHTLHFITLVGTQGRHAGGHG IEFAPMYKINYSRDGTRWISWRNRHGKQVLDGNSNPYDIFLKD LEPPIVARFVRFIPVTDHSMNVCMRVELYGCVWLDGLVSYNAP AGQQFVLPGGSIIYLNDSVYDGAVGYSMTEGLGQLTDGVSGLD DFTQTHEYHVWPGYDYVGWRNESATNGYIEIMFEFDRIRNFTT MKVHCNNMFAKGVKIFKEVQCYFRSEASEWEPNAISFPLVLDD VNPSARFVTVPLHHRMASAIKCQYHFADTWMMFSEITFQSDAA MYNNSEALPTSPMAPTTYDPMLKVDDSNTRILIGCLVAIIFIL LAIIVIILWRQFWQKMLEKASRRMLDDEMTVSLSLPSDSSMFN NNRSSSPSEQGSNSTYDRIFPLRPDYQEPSRLIRKLPEFAPGE EESGCSGVVKPVQPSGPEGVPHYAEADIVNLQGVTGGNTYSVP AVTMDLLSGKRCGCGREFPPGKLLTFKEKLGEGQFGEVHLCEV EGMEKFKDKDFALDVSANQPVLVAVKMLRADANKNARNDFLKE IKIMSRLKDPNIIHLLSVCITDDPLCMITEYMENGDLNQFLSR HEPPNSSSSDVRTVSYTNLKFMATQIASGMKYLSSLNFVHRDL ATRNCLVGKNYTIKIADFGMSRNLYSGDYYRIQGRAVLPIRWM SWESILLGKFTTASDVWAFG\VTLWE\TFTFCQRKGPYS\QLS \DETGY*RNTGEFFPRPKGGQTYLPSTSPFVPDSCVIKLMLSC WRRDTKNRPSFQEIHLLLLQQGDERCCQCLAMFLRLRSSLQDL PLTHAYATPSGHLMKLRDRGLFALPSFPGHPHSLPLTHIYFFF FTLKN
341	1080	916	3	CSASPLRPGLLAPDLLYLPGAGQPRRPEAEPGQKPVVPTLYVT EAEAHSPALPGLSGPQPKWVEVEETIEVRVKKMGPQGVSPTTE VPRSSSGHLFTLPGATPGGDPNSNNSNNKLLAQEAWAQGTAMV GVREPLVFRVDARGSVDWAASGMGSLEEEGTMEEAGEEEGEDG DAFVTEESQDTHSLGDRDPKILTHNGRMLTLADLEDYVPGEGE TFHCGGPGPGAPDDPPCEVSVIQREIGEPTVG\SLCCSAWGMH WVPEALSASLGLSPMGR\HHRDPRSVALRAPPSSCGRPRLGLW AVLPG
342	1081	862	444	QGLAAEFLQVPAVTRAYTAACVLTTAAVQLELLSPFQLYFNPH LVFRKFQAPFLPWALMGFSLLLGNSILVDLLGIAVGHIYYFLE DVFPNQPGGKRLLQTPGFLGLQSSKAPAGSSLTIWTQQSQGGP GTAGELAAPS

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343	1082	3658	337	EKNALEPTVYFGMGV*APQVPRFQQRITGYQYYLQLRKDIWEE GIPCTLEQPIHLAGLAVQAIFGDFDQYESQDFLQKFALFPVGW LQDEKVLEEATQKVALLHQKYRGLTAPDAEMLYMQEVERMDGY GEESYPAKDSQGSDISIGACLEGIFVKHKNGRHPVVFRWHDIA NMSHNKSFFALELANKEETIQFQTEDMETAKYIWRLCVARHKF YRLNQCNLQTQTVTVNPIRRRSSSRMSLPKPQPYVMPPPP\QL HYNGHYTEPYASSQDNLFVPNQEG\YYGQFQTSLNRAQIDFNG RIR\NASVYSAHSTNSLNNPQPYLQPSPMSSNPSITGSDVMRP DYLPSHRHSAVIPPSYRPTPDYETVMKQLNRGLVHAERQSHSL RNLNIGSSYAYSRPAALVYSQPEIREHAQLPSPAAAHCPFSLS YSFHSPSPYPYPAERRPVVGAVSVPELTNAQLQAQDYPSPNIM RTQVYRPPPPYPPPRPANSTPDLSRHLYISSSNPDLITRRVHH SVQTFQEDSLPVAHSLQEVSEPLTAARHAQLHKRNSIEVAGLS HGLEGLRLKERTLSASAAEV\APRAVSVGSQP\SVFTERTQRE GPEEAEGLRYGHKKSLSDATMLIHSSEEEEDEDFEEESGARAP PARAREPRPGLAQDPPGCPRVLLAGPLHILEPKAHVPDAEKRM MDSSPVRTTAEAQRPWRDGLLMPSMSESDLTTSGRYRARRDSL KKRPVSDLLSGKKNIVEGLPPLGGMKKTRVDAKKIGPLKLAAL NGLSLSRVPLPDEGKEVATRATNDERCKILEQRLEQGMVFTEY ERILKKRLVDGECSTARLPENAERNRFQDVLPYDDVRVELVPT KENNTGYINASHIKVSVSGIEWDYIATQGPLQNTCQDFWQMVW EQGIAIIAMVTAEEEGGREKSFRYWPRLGSRHNTVTYGRFKIT TRFRTDSGCYATTGLKMKHLLTGQERTVWHLQYTDWPEHGCPE DLKGFLSYLEEIQSVRRHTNSTSDPQSPNPPLLVHCSAGVGRT GVVILSEIMIACLEHNEVLDIPRVLDMLR\QQRMMLVQTLCQY TFVYRVLIQVPEKAPRLILSSPQFPYGAQSCEAFTA
344	1083	6	304	RKKQKLAEE*VELSKLADLKDAEAVQKFFLEEI*L\GEEILAK GVDHLTNPSAVCGQPQWLLQVLQQTLPLPVIQMLLTKPLPVNQ RLVSAG/SLAKDDVE
345	1084	1255	635	SFCLHEFGWLGSSPQSDHPVPALLGLGAFVHHSLLQVHSSPGA GPVSFLFLGESCSPVDEPRCVPSCAFGFLSCFPLLNSAALERG LFFFVVFFFLESGSCQVARAGVRD/RDRGSLQPPPPGLKQFCL SLPSRWDHRHPPPLRVP*FVFVFLVELGFHHVAQAGLKLLTLS DPPAPASHSAGITGVSQRDQPVLFLRWASCSELVG
346	1085	116	415	EGFPGRSLSGGLCCRLRRRFPIDGYRPRRRRRWSCCPSGVRPV RRMSQKSWIESTLTKRECVYIIPSSKDPHRCLPGCQICQQLVR RGFTVLARMVSIS
347	1086	918	760	QNSTCLTAQTHSLLQHQPLQLTTLLDQYIREQREKDSVMSANG KPDPDTVPDS

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348	1087	1	750	LNPWKNALQDFCLPFLRITSLLQHHLFGEDLPSCQEEEEFSVL ASCLGLLPTFYQTEHPFISASCLDWPVPAFDIITHWCFEIKSF TERHAEQGKALLIQESKWKLPHLLQLPENYNTIFQYYHRKTCS VCTKVPKDPAVCLVCGTFVCLKGLCCKQQSYCECVLHSQNCGA GTGIFLLINASVIIIIRGHRFCLWGSVYLDAHGEEDRDLRRGK PLYICKERYKVLEQQWISHTFDHINKRWGPHYNGL
349	1088	3	1374	KGQLVNLLPPENFPWCGGSQGPRMLRTCYVLCSQAGPRSRGWQ SLSFDGGAFHLKGTGELTRALLVLRLCAWPPLVTHGLLLQAWS RRLLGSRLSGAFLRASVYGQFVAGETAEEVKGCVQQLRTLSLR PLLAVPTEEEPDSAAKSGEAWYEGNLGAMLRCVDLSRGLLEPP SLAEASLMQLKVTALTSTRLCKELASWVRRPGASLELSPERLA EAMDSGQNLQVSCLNAEQNQHLRASLSRLHRVAQYARAQHVRL LVDAEYTSLNPALSLLVAALAVRWNSPGEGGPWVWNTYQACLK DTFERLGRDAEAAHRAGLAFGVKLVRGAYLDKERAVAQL\HG\ MEDPPTQADYEATS\QSYS\RCLELMLTHVARHGPMCHLMVAS HNEESVRQATK\GQAGYVVYKSIPYGSLEEVIPYLIRRAQENR SVLQGARREQELLSQKLWRRLLPGCRRIPH
350	1089	1036	306	VVEFGEMSTARAPEGLRWFQLYVHPDLQLNKQLIQRVESLGFK ALVITLDTPVCGNRRHDIRNQLRRNLTLTDLQSPKKGNAIPYF QMTPISTSLCWNDLSWFQSITRLPIILKGILTKEDAELAVKHN VQGIIVSNHGGRQLDEVLASIDALTEVGAAE*GNMKYYLDAGV RTGNDVQKALALGAKCIFLGRPILWGLACKGEHGVKEVLNILT NEFHTSMA\LTGCRSVAEINRNLVQFSRL
351	1090	1229	957	FFLRWSFTL\LPRLE/CQWLNLGSLQPPPPGFK*SSCLRLLSS WGLQVPTSMLG*FFCIFSREGISPCWPGWSQTPKVIHLPRPPR VLRLQA
352	1091	1145	365	LLCFVHTALQSFQGELYEPHVVIAIVVFLVKLGICK*RASWRK KVTLVVK*S/LKICFTKYGSCYHPGEKSSSWLFN*RMVNDCLA TSCSNRSFVIQQIPSSNLFMVVVDSSCLCESVAPITMAPIEIR YILLCAGPLTTTETSKGYQW*GNLGEKY*RRKITSFPLLERES S*ESCHCQILTSEMQSRKKQSLETCLNYSQHNESLKCERLKAQ KIRRRPESCHGFHPEENARECGGAPSLQAQTVLLLLPLLLMLF SR
353	1092	1140	790	VPSPTHDPKPAEAPMPA*PAPPGPASPGGALEPPAAARAGGSP TAVRSILTKERRPEGGYKAVWFGEDIGTEADVVVLNAPTLDVD GASDSGSGDEGEGAGRGGGPYDAPGGDDSYI

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354	1093	3	2293	LISLAGPTDDIQSTGPQVHALNILRALFRDTRLGENIIPYVAD GAKAAILGFTSPVWAVRNSSTLLFSALITRIFGVKRAKDEHSK TNRMTGREFFSRFPELYPFLLKQLETVANTVDSDMGEPNRHPS MFLLLLVLERLYASPMDGTSSALSMGPFVPFIMRCGHSPVYHS REMAARALVPFVMIDHIPNTIRTLLSTLPSCTDQCFRQNHIHG TLLQVFHLVQAYSDSKHGTNSDFQHELTDITVCTKAKLWLAKR QNPCLVTRAVYIDILFLLTCCLNRSAKDNQPVLESLGFWEEVR GIISGSELITGFPWAFKVPGLPQYLQSLTRLAIAAVWAAAAKS GERETNVPISFSQLLESAFPEVRSLTLEALLEKFLAAASGLGE KGVPPLLCNMGEKFLLLAMKENHPECFCKILKILHCMDPGEWL PQTEHCVHLTPKEFLIWTMDIASNERSEIQSVALRLASKVISH HMQTCVENRELIAAELKQWVQLVILSCEDHLPTESRLAVVEVL TSTTPLFLTNPHPILELQDTLALWKCVLTLLQSEEQAVRDAAT ETVTTAMSQENTCQSTEFAFCQVDASIALALALAVLCDLLQQW DQLAPGLPILLGWLLGESDDLVACVESMHQVEEDYLFEKAEVN FWAETLIFVKYLCKHLFCLLSKSGWRPPSPEMLCHLQRMVSEQ C\HLLSQFFRELPPAAEFVKTVEFTRLRIQEERTLACLRLLAF LEGKEGEDTLVLSVWDSYAESRQLTLPRTEAAC
355	1094	25	1265	HAFRPIALQRGVSFRGCSNQYAESRRLQGESGSRAFAHLMESL LQHLDRFSELLAVSSTTYVSTWDPATVRRALQWARYLRHIHRR FGRHGPIRTALERRLHNQWRQEGGFGRGPVPGLANFQALGHCD VLLSLRLLENRALGDAARYHLVQQLFPGPGVRDADEETLQESL ARLARRRSAVHMLRFNGYRENPNLQEDSLMKTQAELLLERLQE VGKAEAERPARFLSSLWERLPQNNFLKVIAVALLQPPLSRRPQ EELEPGIHKSPGEGSQVLVHWLLGNSEVFAAFCRALPAGLLTL VTSRHPALSPVYLGLLTDWGQRLHYDLQKGIWVGTESQDVPWE ELHNRFQSLCQAPPPLKDKVLTALETCKAQDGDFEEPGLSIWT DLLLALRSGAFRKRQVLGLSAGLSSV
356	1095	3	1027	SHLIQHQRIHT*E*AHECNECGKAFSQTSCLIQHHKMHRKEKS YECNEYEGSFSHSSDLILQQEVLTRQKAFDCDVWEKNSSQRAH LVQHQSIHTKE/K/PHECNEDGKIF/NQIQA/LIQHLRVHTRE K\YVCTACGKAFSHSSAIAQHQIIHTREKPSECDE*RKGISVK LLIDSC/RIYTSEKSYKCIECGKFFMLLVFSYLSHIWRIHMGI KFHCCNECEKAISQRNYLV*YQIHAMQKDYKCN/EACMCVRRF SHNPTLIQHQRIYT*ENLFGCSK/C/GRSFNRSLTSLCHIRIS I/RRQEFDVTQMEKLDTTFQA/STQHRNNGEKIVDYLFMKLLI HSPNLFHCTKI
357	1096	2638	2867	AVTLTAKICSFTPEPSETMSPPAGTNNSRHAALRAVTLPVKVC SFTPEPARSRTHQKEETPNTSEHQKEQTPEAPP

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358	1097	4747	4550	MAYSWQTDPNPNESHEKQYEHQEFLFVNQPHSSSQVSLGFDQI VDEISGKIPHYESEIDENTFFVPTAPKWDSTGHSLNEAHQISL NEFTSKSRELSWHQVSKAPAIGFSPSVLPKPQNTNKECSWGSP IGKHHGADDSRFSILAPSFTSLDKINLEKELENENHNYHIGFE SSIPPTNSSFSSDFMPKEENKRSGHVNIVEPSLMLLKGSLQPG MWESTWQKNIESIGCSIQLVEVPQSSNTSLASFCNKVKKIRER YHAADVNFNSGKIWSTTTAFPYQLFSKTKFNIHIFIDNSTQPL HFMPCANYLVKDLIAEILHFCTNDQLLPKDHILSVWGSEEFLQ NDHCLGSHKMFQKDKSVIQLHLQKSREAPGKLSRKHEEDHSQF YLNQLLEFMHIWKVSRQCLLTLIRKYDFHLKYLLKTQENVYNI IEEVKKICSVLGCVETKQITDAVNELSLILQRKGENFYQSSET SAKGLIEKVTTELSTSIYQLINVYCNSFYADFQPVNVPRCTSY LNPGLPSHLSFTVYAAHNIPETWVHRINFPLEIKSLPRESMLT VKLFGIACATNNANLLAWTCLPLFPKEKSILGSMLFSMTLQSE PPVEMITPGVWDVSQPSPVTLQIDFPATGWEYMKPDSEENRSN LEEPLKECIKHIARLSQKQTPLLLSEEKKRYLWFYRFYCNNEN CSLPLVLGSAPGWDERTVSEMHTILRRWTFSQPLEALGLLTSS FPDQEIRKVAVQQLDNLLNDELLEYLPQLVQAVKFEWNLESPL VQLLLHRSLQSIQVAHRLYWLLKNAENEAYFKSWYQKLLAALQ FCAGKALNDEFSKEQKLIKILGDIGERVKSASDHQRQEVLKKE IGRLEEFFQDVNTCHLPLNPALCIKGIDHDACSYFTSNALPLK ITFINANLMGKNISIIFKAGDDLRQDMLVLQLIQVMDNIWLQE GLDMQMIIYRCLSTGKDQRLVQMVPDAVTLAKIHRHSGLIGPL KENTIKKWFSQHNHLKADYEKALRNFFYSCAGWCVVTFILGVC DRHNDNIMLTKSGHMFHIDFGKFLGHAQTFGGIKRDRAPFIFT SEM\EYFITEGG\KNPQHFQDFV\ELCCRAYNIIRKHSQLLL\ NLL\EMMLYAG\LPELSGI\QDLKYVYNNLRPQDTDLEATSHF TKKIKESLECFPVKLNNLIHTLAQMSAISPAKSTSQTFPQESC LLSTTRSIERATILGFSKKSSNLYLIQVTHSNNETSLTEKSFE QFSKLHSQLQKQFASLTLPEFPHWWHLPFTNSDHRRFRDLNHY MEQILNVSHEVTNSDCVLSFFLSEAGQQTVEESSPVYLGEKFP DKKPKVQLVISYEDVKLTILVKHMKNIHLPDGSAPSAHVEFYL LPYPSEVRRRKTKSVPKCTDPTYNEIVVYDEVTELQGHVLMLI VKSKTVFVGAINIRLCSVPLDKEKWYPLGNSII*PLLLFYTSN FMQSVLH
359	1098	679	346	FFLRWSLDSVTQAGVQSHDLSSLQPPPPGFKQSSLFGLPSSWE *RWVPPCPANFFVFLVETGFRHVGQAGLELLTSNDLPVSACQS AGITGVTTVPQRKSMILYEVTICYP

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360	1099	2	1601	FVREIRGPAVPRLTSAEDRHRHGPHAHSPELQRTGRDYSLDYL PFRLWVGIWVATFCLVLVATEASVLVRYFTRFTEEGFCALISL IFIYDAVGKMLNLTHTYPIQKPGSSAYGCLCQYPGPGGNESQW IRTRPKDRDDIVSMDLGLINASLLPPPECTRQGGHPRGPGCHT VPDIAFFSLLLFLTSFFFAMALKCVKTSRFFPSVVRKGLSDFS SVLAILLGCGLDAFLGLATPKLMVPREFKPTLPGRGWLVSPFG ANPWWWSVAAALPALLLSILIFMDQQITAVILNRMEYRLQKGA GFHLDLFWVAVLMLLTSALGLPWYVSATVISLAHMDSLRRESR ACAPGERPNFLGIREQRLTGLVVFILTGASIFLAPVLKFIPMP VLYGIFLYMGVAALSSIQFTNRVKLLL\MPAKHQPDLLLLRHV PLTRVHLFTAISFA\CLGLLW\IIKSTPAAIIFPLMLLGLVGV RKALERVFSPQELLWLDELMPEEERSIPEKGLEPEHSFSGSDS EDSELMYQPKAPEINISVN*LE*EFVREIRGPAVPRLTSAEDR HRHGPHAHSPELQRTGRDYSLDYLPFRLWVGIWVATFCLVLVA TEASVLVRYFTRFTEEGFCALISLIFIYDAVGKMLNLTHTYPI QKPGSSAYGCLCQYPGPGGNESQWIRTRPKDRDDIVSMDLGLI NASLLPPPECTRQGGHPRGPGCHTVPDIAFFSLLLFLTSFFFA MALKCVKTSRFFPSVVRKGLSDFSSVLAILLGCGLDAFLGLAT PKLMVPREFKPTLPGRGWLVSPFGANPWWWSVAAALPALLLSI LIFMDQQITAVILNRMEYRLQKGAGFHLDLFCVAVLMLLTSAL GLPWYVSATVISLAHMDSLRRESRACAPGERPNFLGIREQRLT GLVVFILTGASIFLAPVLKFIPMPVLYGIFLYMGVAALSSIQF TNRVKLLLDASKTPARPATLAACASDQGPPLHSHQLCPVWGCF GIIKSTPAAIIFPLMLLGLVGVRKALERVFSPQELLWLDELMP EEERSIPEKGLEPEHSFSGSDSEDSELMYQPKAPEINISVN

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361	1100	1	2636	MGLKARRAAGAAGGGGDGGGGGGGAANPAGGDAAAAGDEERKV GLAPGDVEQVTLALGAGADKDGTLLLEGGGRDEGQRRTPQGIG LLAKTPLSRPVKRNNAKYRRIQTLIYDALERPRGWALLYH\AL VFLIVLG\CLILAVL\TTFKEYETVSGDWLLLLETFAIFIFGA EFALRIWAAGCCCRYKGWRGRLKFARKPLCMLDIFVLIASVPV VAVGNQGNVLATSLRSLRFLQILRMLRDGPGEGGTWKLLG\SA ICAHSKELITAWYIGFLTLILSSFLVYLVEKDVPEVDAQGEEM KEEFETYADALWWGLITLATIGYGDKTPKTWEGRLIAATFSLI GVSFFALPAGILGSGLALKVQEQHRQKHFEKRRKPAAELIQAA WRYYATNPNRIDLVATWRFYESVVSFPFFRKEQLEAASSQKLG LLDRVRLSNPRGSNTKGKLFTPLNVDAIEESPSKEPKPVGLNN KERFRTAFRMKAYAFWQSSEDAGTGDPMAEDRGYGNDFPIEDM IPTLKAAIRAVRILQFRLYKKKFKETLRPYDVKDVIEQYSAGH LDMLSRIKYLQTRIDMIFTPGPPSTPKHKKSQKGSAFTFPSQQ SPRNEPYV\ARPST\SEI\EDQRH*WGKFVKSLKGQV\QGLGR KLDFLVDMHMQHMERLQVQVTEYYPTKGTSSPAEAEKKEDNRY SDLKTIICNYSETGPPEPPYSFHQVTIDKVSPYGFFAHDPVNL PRGGPSSGKVQATPPSSATTYVERPTVLPILTLLDSRVSCHSQ ADLQGPYSDRISPRQRRSITRDSDTPLSLMSVNHEELERSPSG FSISQDRDDYVFGPNGGSSWMREKRYLAEGETDTDTDPFTPSG SMP\LSSTGDGISDSVWTPSNKPI

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362	1101	1	5433	RTRGIIEFDPKYTAFEVEEDVGLIMIPVVRLHGTYGYVTADFISQSSSASPGG VDYILHGSTVTFQHGQNLSFINISIIDDNESEFEEPIEILLTGATGGAVLGRH LVSRIIIAKSDSPFGVIRFLNQSKISIANPNSTMILSLVLERTGGLLGEIQVN WETVGPNSQEALLPQNRDIADPVSGLFYFGEGEGGVRTIILTIYPHEEIEVEE TFIIKLHLVKGEAKLDSRAKDVTLTIQEFGDPNGVVQFAPETLSKKTYSEPLA LEGPLLITFFVRRVKGTFGEIMVYWELSSEFDITEDFLSTSGFFTIADGESEA SFDVHLLPDEVPEIEEDYVIQLVSVEGGAELDLEKSITWFSVYANDDPHGVFA LYSDRQSILIGQNLIRSIQINITRLAGTFGDVAVGLRISSDHKEQRIVTENAE RQLVVKDGATYKVDVVPIKNQVFLSLGSNFTLQLVTVMLVGGRFYGMPTILQE AKSAVLPVSEKAANSQVGFESTAFQLMNITAGTSHVMISRRGTYGALSVAWTT GYAPGLEIPEFIVVGNMTPTLGSLSFSHGEQRKGVFLWTFPSPGWPEAFVLHL SGVQSSAPGGAQLRSGFIVAEIEPMGVFQFSTSSRNIIVSEDTQMIRLHVQRL FGFHSDLIKVSYQTTAGSAKPLEDFEPVQNGELFFQKFQTEVDFEITIINDQL SEIEEFFYINLTSVEIRGLQKFDVNWSPRLNLDFSVAVITILDNDDLAGMDIS FPETTVAVAVDTTLIPVETESTTYLSTSKTTTILQPTNVVAIVTEATGVSAIP EKLVTLHGTPAVSEKPDVATVTANVSIHGTFSLGPSIVYIEEEMKNGTFNTAE VLIRRTGGFTGNVSITVKTFGERCAQMEPNALPFRGIYGISNLTWAVEEEDFE EQTLTLIFLDGERERKVSVQILDDDEPEGQEFFYVFLTNPQGGAQIVEGKDDT GFAAFAMVIITGSDLHNGIIGFSEESQSGLELREGAVMRRLHLIVTRQPNRAF EDVKVFWRVTLNKTVVVLQKDGVNLMEELQSVSGTTTCTMGQTKCFISIELKP EKVPQVEVYFFVELYEATAGAAINNSARFAQIKILESDESQSLVYFSVGSRLA VAHKKATLISLQVARDSGTGLMMSVNFSTQELRSAETIGRTIISPAISGKDFV ITEGTLVFEPGQRSTVLDVILTPETGSLNSFPKRFQIVLFDPKGGARIDKVYG TANITLVSDADSQAIWGLADQLHQPVNDDILNRVLHTISMKVATENTDEQLSA MMHLIEKITTEGKIQAFSVASRTLFYEILCSLINPKRKDTRGFSHFAELTENF AFSLLTNVTCGSPGEKSKTILDSCPYLSILALHWYPQQINGHKFEGKEGDYIR IPERLLDVQDAEIMAGKSTCKLVQFTEYSSQQWFISGNNLPTLKNKVLSLSVK GQSSQLLTNDNEVLYRIYAAEPRIIPQTSLCLLWNQAAASWLSDSQFCKVIEE TADYVECACLHMSVYAVYARTDNLSSYNEAFFTSGFICISGLCLAVLSHIFCA RYSMFAAKLLTHMMAASLGTQILFLASAYASPQLAEESCSAMAAVTHYLYLCQ FSWMLIQSVNFWYVLVMNDEHTERRYLLFFLLSWGLPAFVVILLIVILKGIYH QSMSQIYGLIHGDLCFIPNVYAALFTAALVPLTCLVVVFVVFIHAYQVKPQWK AYDDVFRGRTNAAEIPLILYLFALISVTWLWGGLHMAYRHFWMLVLFVIFNSL QLL\YPLFYFLLL*DQSSSASPGGVDYILHGSTVTFQHGQNLSFINISIIDDN ESEFEEPIEILLTGATGGAVLGRHLVSRIIIAKSDSPFGVIRFLNQSKISIAN PNSTMILSLVLERTGGLLGEIQVNWETVGPNSQEALLPQNRDIADPVSGLFYF GEGEGGVRTIILTIYPHEEIEVEETFIIKLHLVKGEAKLDSRAKDVTLTIQEF GDPNGVVQFAPETLSKKTYSEPLALEGPLLITFFVRRVKGTFGEIMVYWELSS EFDITEDFLSTSGFFTIADGESEASFDVHLLPDEVPEIEEDYVIQLVSVEGGA ELDLEKSITWFSVYANDDPHGVFALYSDRQSILIGQNLIRSIQINITRLAGTF GDVAVGLRISSDHKEQPIVTENAERQLVVKDGATYKVDVVPIKNQVFLSLGSN FTLQLVTVMLVGGRFYGMPTILQEAKSAVLPVSEKAANSQVGFESTAFQLMNI TAGTSHVMISRRGTYGALSVAWTTGYAPGLEIPEFIVVGNMTPTLGSLSFSHG EQRKGVFLWTFPSPGWPEAFVLHLSGVQSSAPGGAQLRSGFIVAEIEPMGVFQ FSTSSRNIIVSEDTQMIRLHVQRLFGFHSDLIKVSYQTTAGSAKPLEDFEPVQ NGELFFQKFQTEVDFEITIINDQLSEIEEFFYINLTSVEIRGLQKFDVNWSPR LNLDFSVAVITILDNDDLAGMDISFPETTVAVAVDTTLIPVETESTTYLSTSK TTTILQPTNVVAIVTEATGVSAIPEKLVTLHGTPAVSEKPDVATVTANVSIHG TFSLGPSIVYIEEEMKNGTFNTAEVLIRRTGGFTGNVSITVKTFGERCAQMEP NALPFRGIYGISNLTWAVEEEDFEEQTLTLIFLDGERERKVSVQILDDDEPEG QEFFYVFLTNPQGGAQIVEGKDDTGFAAFAMVIITGSDLHNGIIGFSEESQSG LELREGAVMRRLHLIVTRQPNRAFEDVKVFWRVTLNKTVVVLQKDGVNLMEEL QSVSGTTTCTMGQTKCFISIELKPEKVPQVEVYFFVELYEATAGAAINNSARF AQIKILESDESQSLVYFSVGSRLAVAHKKATLISLQVARDSGTGLMMSVNFST QELRSAETIGRTIISPAISGKDFVITEGTLVFEPGQRSTVLDVILTPETGSLN SFPKRFQIVLFDPKGGARIDKVYGTANITLVSDADSQAIWGLADQLHQPVNDD ILNRVLHTISMKVATENTDEQLSAMMHLIEKITTEGKIQAFSVASRTLFYEIL CSLINPKRKDTRGFSHFAELTENFAPSLLTNVTCGSPGEKSKTILDSCPYLSI LALHWYPQQINGHKFEGKEGDYIRIPERLLDVQDAEIMAGKSTCKLVQFTEYS SQQWFISGNNLPTLKNKVLSLSVKGQSSQLLTNDNEVLYRIYAAEPRIIPQTS LCLLWNQAAASWLSDSQFCKVIEETADYVECACLHMSVYAVYARTDNLSSYNE AFFTSGFICISGLCLAVLSHIFCARYSMFAAKLLTHMMAASLGTQILFLASAY ASPQLAEESCSAMAAVTHYLYLCQFSWMLIQSVNFWYVLVMNDEHTERRYLLF FLLSWGLPAFVVILLIVILKGIYHQSMSQIYGLIHGDLCFIPNVYAALFTAAL VPLTCLVVVFVVFIHAYQVKPQWKAYDDVFRGRTNAAEIPLILYLFALISVTW LWGGLHMAYRHFWMLVLFVIFNSLQLLVPSVLLFTSMRSTFFSFHTGTLTSRE KKSTFVLTCLLSPDSKGLGVLCFLNTEWAFQVH

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363	1102	2	2855	AAGATMERDGCAGGGSRGGEGGRAPREGPAGNGRDRGRSHAAE APGDPQAAASLLAPMDVGEEPLEKAARARTAKDPNTYKVLSLV LSVCVLTTILGCIFGLKPSCAKEVKSCKGRCFERTFG\NCRCD AACVELG\NCCLGLPGGTCI\EP\EHIW\TCNKFRCG\EKRLT RSLCACSDDCKD\RGDCLPSNLQFLCVQGE\KSWGRKNPCESH LMEP\QCP\AGFETPSLPLLIF/SLDGFRAEYLHTWGGLLPVI SKLKKCGTYTKNMRPVYPTKTFPNHYSIVTGLYPESHGIINNK MYDPKMNASFSLKSKEKFNPEWYKGEPIWVTAKYQGLKSGTFF WPGSDVEINGIFPDIYKMYNGSVPFEERILAVLQWLQLPKDER PHFYTLYLEEPDSSGHSYGPVSSEVIKALQRVDGMVGMLMDGL KELNLHRCLNLILISDHGMEQGSCKKYIYLNKYLGDVKNIKVI YGPAARLRPSDVPDKYYSFNYEGIARNLSCREPNQHFKPYLKH FLPKRLHFAKSDRIEPLTFYLDPQWQLALNPSERKYCGSGFHG SDNVFSNMQALFVGYGPGFKHGIEADTFENIEVYNLMCDLLNL TPAPNNGTHGSLNHLLKNPVYTPKHPKEVHPLVQCPFTRNPRD NLGCSCNPSILPIEDFQTQFNLTVAEEKIIKHETLPYGRPRVL QKENTICLLSQHQFMSGYSQDILMPLWTSYTVDRNDSFSTEDF SNCLYQDFRIPLSPVHKCSFYKNNTKVSYGFLSPPQLNKNSSG IYSEALLTTNIVPMYQSFQVIWRYFHDTLLRKYAEERNGVNVV SGPVFDFDYDG\RCDSL\ENLRQKRRVHPVTQENFWIPNSTSF Y/VVLTSC\KDTSQTPLHC\ENL\DTLGFPFCLHRDWINSETC \VHG\KHDSSW\VEEFVKCLHRA\RITGC*GTSLGLSFYQQRK EPVSDILKLKTHLPTFSQED
364	1103	657	1	TVPPPPGGPSPAPLHPKRSPTSTGEAELKEERLPGRKASCSTA GSGSRGLPPL\SPMVSSAHNPNKAEIPERRKDSTSTPNNLPPS MMTRRNTYVCTERPGAERPSLLPNGKENSSGTPRVPPASPSSH SLAPPSGERSRLARGSTIRSTFHGGQVRDRRAGGWGWFFNKHA LQRAPRNAGAPSLMPGHRTVLINYGGGQDLKNWETCLAAPPNK HRR
365	1104	1	1313	HTLHHSSPTSEAEEFVSRLSTQNYFRSLPRGTSNMTYGTFNFL GGRLMIPNTGISLLIPPDAIPRGKIYEIYLTLHKPEDVRLPLA GCQTLLSPIVSCGPPG\VLLTRPVILG\MDHCG\EPSPDSW\S LRLKKQSCEGSWEDVLHLGEEAPSHLYYCQLEASACYVFTEQL SRYALVGEALSVAAAKRLKLLLFAPVACTSLEYNILVYCLHDT HDALNVVVQLEKQLQGQLIQEPLVLHFKDSYHNLRLSIHDVPS SLWKSKLLVSYQEIPFYHIWNGTQRYLHCTFTLERVSPSTSDL ACKLWVWQVEGDGQSFSINFNITKDTRFAELLALESEAGVPAL VGPSAFKIPFLIRQKIISSLDPPCRRGADWRTLAQKLHLDSHL SFFASKPSPTAMILNLWEARHFPNGNLSQLAAAVAGTGPAGRW LLSQCSEAEC
366	1105	1	343	GSAAGQVQQQQQRRHQQGKVTVKYDRKELRKRLVLEEWIVEQL GQLYGCEEEEMPEVEIDIDDLFDAYSDEQRASKLQEALVDCYK PTEEFIKELLSRIRGMRKLSP\PQKKSV

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367	1106	2	1398	IMLDGRVRWLTPVISALWEAEMEDVIARMQDEKNGIPIRTVKS FLSKIPSVFSGSDIVQWLIKNLTIEDPVEALHLGTLMAAHGYF FPISDHVLTLKDDGTFYRFQTPYFWPSNCWEPENTDYAVYLCK RTMQNKARLELADYEAESLARLQRAFARKWEFIFMQAEAQAKV DKKRDKIERKILDSQERAFWDVHRPVPGCVNTTEVDIKKSSRM RNPHKTRKSVYGLQNDIRSHSPTHTPTPETKPPTEDELQQQIK YWQIQLDRHRLKMSKVADSLLSYTEQYLEYDPFLLPPDPSNPW LSDDTTFWELEASKEPSQQRVKRWGFGMDEALKDPVGREQFLK FLESEFSSENLRFWLAVEDLKKRPIKEVPSRVQEIWQEFLAPG APSAINLDSKSYDKTTQNVKEPGRYTFEDAQEHIYKLMKSDSY PRFIRSSAYQELLQAKK\KGKSLTSKRLTSLAQSY
368	1107	1	461	GTRDYPRIVNHLDHTYVTAPQAFMMFQYFVKVVPTVYMKVDGE VLTTNQIYVTRHEKAAYVLMGDQGLPGVFILYELSPMMVNLTE IHTFFSLFLTIVGA\TIGGMFFEHFVINYLTHKWGLGFYFKNE NSLQGGHRTLYGVNFFMYWSLRGGS
369	1108	2	1522	SVWWNSQRQFVVRAWGCAGPCGRAVFLAFGLGLGLIEEKQAES RRAVSACQEIQAIFTQKSKPGPDPLDTRRLQGFRLEEYLIGQS IGKGCSAAVYEATMPTLPQNLEVTKSTGLLPGRGPGTSAPGEG QERAPGAPAFPLAIKMMWNISAGSSSEAILNTMSQELVPASRV ALAGEYGAVTYRKSKRGPKQLAPHPNIIRVLRAFTSSVPLLPG ALVDYPDVLPSRLHPEGLGHGRTLFLVMKNYPCTLRQYLCVNT PSPRLAAMMLLQLLEGVDHLVQQGIAHRDLKSDNILVELDPDG CPWLVIADFGCCLADESIGLQLPFSSWYVDRGGNGCLMAPEVS TARPGPRAVIDYSKADAWAVGAIAYEIFGLVNPFYGQGKAHLE SRSYQEAQLPALPESVPPDVRQLVRALLQREASKRPSARVAAN VLHLSLWGEHILALKNLKLDKMVGWLLQQSAATLLANRLTEKC CVETKMKMLFLANLECETLCQAALLLCSWRAAL
370	1109	105	1252	RPLLRLAELPDHCYRMNSSPAGTPSPQPSRANGNINLGPSANP NAQPTDFDFLKVIGKGNYGKVLLAKRKSDGAFYAVKVLQKKSI LKKKEQSHIMAERSVLLKNVRHPFLVGLRYSFQTPEKLYFVLD YVNGGELFFHLQRERRFLEPRARFYAAEVASAIGYLHSLNIIY RDLKPENILLDCQGHVVLTDFGLCKEGVEPEDTTSTFCGTPEY LAPEVL\RKEPYDRAVDWWCLGAVLYEMLHGLPPFYSQDVSQM YENILHQPLQIPGGRTVAACDLLQSLLHKDQRQRLGSKADFLE IKNHVFFSPINWDDLYHKRLTPPFNPNVTGPADLKHFDPEFTQ EAVSKSIGCTPDTVASSSGASSAFLGFSYAPEDDDILDC

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371	1110	3	1608	RPQTLKGHQEKIRQRQSILPPPQGPAPIPFQHRGGDSPEAKNR VGPQVPLSEPGFRRRESQEEPRAVLAQKIEKETQILNCALDDI EWFVARLQKAAEAFKQLNQRKKGKKKGKKAPAEGVLTLRARPP \SEGEFIDCFQKIKLAINLLAKLQKHIQNPSAAELVHFLFGPL DLIVNTCSGPDIARSVSCPLLSRDAVDFLRGHLVPKEMSLWES LGESWMRPRSEWPREPQVPLYVPKFHSGWEPPVDVLQEAPWEV EGLASAPIEEVSPVSRQSIRNSQKHSPTSEPTPPGDALPPVSS PHTHRGYQPTPAMAKYVKILYDFTARNANELSVLKDEVLEVLE DGRQWWKLRSRSGQAGYVPCNILGEARPEDAGAPFEQAGQKYW GPASPTHKLPPSFPGNKDELMQHMDEVNDELIRKISNIRAQPQ RHFRVERSQPVSQPLTYESGPDEVRAWLEAKAFSPRIVENLGI LTGPQLFSLNKEELKKVCGEEGVRVYSQLTMQKAFLEKQQSGS ELEELMNKFHSMNQRRGEDS
372	1111	3	1046	AWHEGLVSSPAIGAYLSASYGDSLVVLVATVVALLDICFILVA VPESLPEKMRPVSWGAQISWKQADPFASLKKVGKDSTVLL\IC ITVCLSYLPEAG\QYSSFF\LYLR\QVIGFG\SVKIAAFIAMV GILSIVAQTAFLSILMRSLGNKNTVLLGLGFQMLQLAWYGFGS QAWMMWAAGTVAAMSSITFPAISALVSRNAESDQQGVAQGIIT GIRGLCNGLGPALYGFIFYMFHVELTELGPKLNSNNVPLQGAV IPGPPFLFGACIVLMSFLAALFIPEYSKASGVQKHSNSSSGSL TNTPERGSDEDIEPLLQDSSIWELSSFEEPGNQCTEL*TRQKV GFCIRHL
373	1112	1	1950	MAAGLATWLPFARAAAVGWLPLAQQPLPPAPGVKASRGDEVLV VNVSGRRFETWKNTLDRYPDTLLGSSEKEFFYDADSGEYFFDR DPDMFRHVLNFYRTGRLHCPRQECIQAFDEELAFYGLVPELVG DCCLEEYRDRKKENAERLAEDEEAEQAGDGPALPAGSSLRQRL WRAFENPHTSTAALVFYYVTGFFIAVSVIANVVETIPCRGSAR RSSREQPCGERFPQAFFCMDTACVLIFTGEYLLRLFAAPSRCR FLRSVMSLIDVVAILPYYIGLLVPKNDDVSGAFVTLRVFRVFR IFKFSRHSQGLRILGYTLKSCASELGFLLFSLTMAIIIFATVM FYAEKGTNKTNFTSIPAAFWYTIVTMTTLGYGDMVPSTIAGKI FGSICSLSGVLVIALPVPVIVSNFSRIYHQNQRADKRRAQQKV RLARIRLAKSGTTNAFLQYKQNGGLEDSGSGEEQAVCVRNRSA FEQQHHHLLHCLEKTTCHEFTDELTFSEALGAVSPGGRTSRST SVSSQPVGPGSLLSSCCPRRAKRRAIRLANSTASVSRG\SMQE LDMLAGL\RRSHAP\QSRSSL\NAKPHDSLDLNCDSG\DFVAA IISIPTPPANTPDESQPSSPGGGGRAGSTLRNSSLGTPCLFPE TVKISSL
374	1113	4	664	GWGKPFKDWTTGGQDTGGEPALLVGAGEGRAPRLNCPSGQIRS PGPGDLSIYDNWIRYFNRSSPVYGLVP/RSKTSARIYPTYHTA FDTFDYVDKFLDPGEEGDKGHPETRTGEAED*ALALSPCRR\F SSHQAVARTAGSVILRLSDSFFLPLKVSDYSETLRSFLQAAQQ DLGALLEQHSISLGPLVTAVEKFEAEAAALGQRISTLQKGSPD PLQVRML

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375	1114	1	1147	GIRGGGSLASGGPGPGHASLSQRLRLYLADSWNQCDLVALTCF LLGVGCRLTPGLYHLGRTVLCIDFMVFTVRLLHIFTVNKQLGP KIVIVSKMMKDVFFFLFFLGVWLVAYGVATEGLLRPRDSDFPS ILRRVFYRPYLQIFGQIPQEDMDVALMEHSNCSSEPGFWAHPP GAQAGTCVSQYANWLVVLLLVIFLLVANILLVNLLIAMFSYTF GKVQGNSDLYWKAQRYRLIREFHSRPALAPPFIVISHLRLLLR QLCRRPRSPQPSSPALEHFRVYLSKEAERKLLTWESVHKENFL LARARDKRESDSERLKRTSQKVDLALKQLGHIREYEQRLKVLE REVQQCSRVLGWVAEALSRSALLPPGGPPPPDLPGSKD
376	1115	3	329	LIKLCKSKAKSCENDLEMGMLNSKFKKTRYQAGMRNSENLTAN NTLSKPTRY/QGELKEIKQDISSLRYELLEEKSQATGELADLI QQLSEKFGKNLNKDHLRVNKGKDI
377	1116	1	2043	LPLLHAGFNRRFMENSSIIACYNELIQIEHGEVRSQFKLRACN SVFTALDHCHEAIEITSDDHVIQYVNPAFERMMGYHKGELLGK ELADLPKSDKNRADLLDTINTCIKKGKEWQGVYYARRKSGDSI QQHVKITPVIGQGGKIRHFVSLKKLCCTTDNNKQIHKIHRDSG DNSQTEPHSFRYKNRRKESIDVKSISSRGSDAPSLQNRRYPSM ARIHSMTIEAPITKVINIINAAQENSPVTVAEALDRVLEILRT TELYSPQLGTKDEDPHTSDLVGGLMTDGLRRLSGNEYVFTKNV HQSHSHLAMPITINDVPPCISQLLDNEESWDFNIFELEAITHK RPLVYLGLKVFSRFGVCEFLNCSETTLRAWFQVIEANYHSSNA YHNSTHAADVLHATAFFLGKERVKGSLDQLDEVAALIAATVHD VDHPGRTNSFL\CNAGSELAVLYNDT\AV\LESHHTALAFQ\L TVKDTK\CNIFKNID/RGNHYRTLRQAIIDMVLATEMTKHFEH VNKFVNSINKPMAAEIEGSDCECNPAGKNFPENQILIKRMMIK CADVANPCRPLDLCIEWAGRISEEYFAQTDEEKRQGLPVVMPV FDRNTCSIPKSQISFIDYFITDMFDAWDAFAHLPALMQHLADN YKHWKTLDDLKCKSLRLPSDRLKPSHRGGLLTDKGHCESQ

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378	1117	1	3585	AFLSKVEEDDYPSEELLEDENAINAKRSKEKNPGNQGRQFDVN LQVPDRAVLGTIHPDPEIEESKQETSMILDSEKTSETAAKGVN TGGREPNTMVEKERPLADKKAQRPFERSDFSDSIKIQTPELGE VFQNKDSDYLKNDNPEEHLKTSGLAGEPEGELSKEDHENTEKY MGTESQGSAAAEPEDDSFHWTPHTSVEPGHSDKREDLLIISSF FKEQQSLQRFQKYFNVHELEALLQEMSSKLKSAQQESLPYNME KVLDKVFRASESQILSIAEKMLDTRVAENRDLGMNENNIFEEA AVLDDIQDLIYFVRYKHSTAEETATLVMAPPLEEGLGGAMEEM QPLHEDNFSREKTAELNVQVPEEPTHLDQRVIGDTHASEVSQK PNTEKDLDPGPVTTEDTPMDAIDANKQPETAAEEPASVTPLEN AILLIYSFMFYLTKSLVATLPDDVQPGPDFYGLPWKPVFITAF LGIASFAIFLWRTVLVVKDRVYQVTEQQISEKLKTIMKENTEL VQKLSNYEQKIKESKKHVQETRKQNMILSDEAIKYKDKIKTLE KNQEILDDTAKNLRVMLESEREQNVKNQDLISENKKSIEKLKD VISMNASEFSEVQIALNEAKLSEEKVKSECHRVQEENARLKKK KEQLQQEIEDWSKLHAELSEQIKSFEKSQKDLEVALTHKDDNI NALTNCITQLNLLECESESEGQNKGGNDSDELANGEVGGDRNE KMKNQIKQMMDVSRTQTAISVVEEDLKLLQLKL\RASVSTKC\ NLEDQVKKLEDDRNSLQAAKAGLEDECKTLRQKVEILNELYQQ KEMALQKKLSQEEYERQEREHRLSAADEKAVSAAEEVKTYKRR IEEMEDELQKTERSFKNQIATHEKKAHENWLKARAAERAIAEE KREAANLRHKLLDLTQKMAMLQEEPVIVKPMPGKPNTQNPPRR GPLSQNGSFGPSPVSGGECSPPLTVEPPVRPLSATLNRRDMPR SEFGSLDGPLPHPRWSAEASGKPSPSDPGSGTATMMNSSSRGS SPTRVLDEGKVNMAPKGPPPFPGVPLMSTPMGGPVPPPIRYGP PPQLCGPFGPRPLPPPFGPGMRPPLGLREFAPGVPPGRRDLPL HPRGFLPGHAPFRPLGSLGPREYFIPGTRLPPPTHGPQEYPPP PAVRDLLPSGSRDEPPPASQSTSQDCSQALKQSP

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379	1118	3	2946	MAADSEPESEVFEITDFTTASEWERFISKVEEVLNDWKLIGNS LGKPLEKGIFTSGTWEEKSDEISFADFKFSVTHHYLVQESTDK EGKDELLEDVVPQSMQDLLGMNNDFPPRAHCLVRWYGLREFVV IAPAAHSDAVLSESKCNLLLSSVSIALGNTGCQVPLFVQIHHK WRRMYVGECQGPGVRTDFEMVHLRKVPNQYTHLSGLLDIFKSK IGCPLTPLPPVSIAIRFTYVLQDWQQYFWPQQPPDIDALVGGE VGGLEFGKLPFGACEDPISELHLATTW\PHLTEGIIVDNDVYS DLDPIQAPHWSVRVRKAENPQCLLGDFVTEFFKICRRKESTDE ILGRSAFEEEGKETADITHALSKLTEPASVPIHKLSVSNMVHT AKKKIRKHRGVEESPLNNDVLNTILLFLFPDAVSEKPLDGTTS TDNNNPPSESEDYNLYNQFKSAPSDSLTYKLALCLCMINFYHG GLKGVAHLWQEFVLEMRFRWENNFLIPGLASGPPDLRCCLLHQ KLQMLNCCIERKKARDEGKKTSASDVTNIYPGDAGKAGDQLVP DNLKETDKEKGEVGKSWDSWSDSEEEFFECLSDTEELKGNGQE SGKKGGPKEMANLRPEGRLYQHGKLTLLHNGEPLYIPVTQEPA PMTEDLLEEQSEVLAKLGTSAEGAHLRARMQSACLLSDMESFK AANPGCSLEDFVRWYSPRDYIEEEVIDEKGNVVLKGELSARMK IPSNMWVEAWETAKPIPARRQRRLFDDTREAEKVLHYLAIQKP ADLARHLLPCVIHAAVLKVKEEESLENISSVKKIIKQIISHSS KVLHFPNPEDKKLEEIIHQITNVEALIARARSLKAKFGTEKCE QEEEKEDLERFVSCLLEQPEVLVTGAGRGHAGRIIHKLFVNAQ RAAAMTPPEEELKRMGSPEERRQNSVSDFPPPAGREFILRTTV PRPAPYSKALPQRMYSVLTKEDFRLAGAFSSDTSFF
380	1119	2333	670	SPTRTGDRSVSLIVFLTEGKPTVGETHTLKILNNTREAARGQV CIFTIGIGNDVDFRLLEKLSLENCGLTRRVHEEEDAGSQLIGF YDEIRTPLLSDIRIDYPPSSVVQATKTLFPNYFNGSEIIIAGK LVDRKLDHLHVEVTASNSKKFIILKTDVPVRPQKAGKDVTGSP RPGGDGEGDTNHIERLWSYLTTKELLSSWLQSDDEPEKERLRQ RAQALAVSYRFLTPFTSMKLRGPVPRMDGLEEAHGMSAAMGPE PVVQSVRGAGTQPGPLLKKPYQPRIKISKTSVDGDPHFVVDFP LSRLTVCFNIDGQPGDILRLVSDHRDSGVTVNGELIGAPAPPN GHKKQRTYLRTITILINKPERSYLEITPSRVILDGGDRLVLPC NQSVVVGSWGLEVSVSANANVTVTIQGSIAFVILIHLYKKPAP FQRHHLGFYIANSEGLSSNCHGLLGQFLNQDARLTEDPAGPSQ NLTHPLLLQVGEGPEAVLTVKGHQVPVVWKQRKIYNGEEQIDC WFARNNAAKLIDGEYKDYLASHPFDTGMTLGQGMSREL
381	1120	102	426	VPLESLSCSHADNWKQELTKFISPDQLPVEFGGTMTDPDGNPK CLTKINYGGEVPKSYYLCKQVRLQYEHTRSVGRGSSLQVENEI LFPGCVLRCPEVLQHLQPGSF

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382	1121	3	3726	PAAPEHTDPSEPRGSVSCCSLLRGLSSGWSSPLLPAPVCNPNK AIFTVDAKTTEILVANDKACGLLGYSSQDLIGQKLTQFFLRSD SDVVEALSEEHMEADGHAAVVFGTVVDIISRSGEKIPVSVWMK RMRQERRLCCVVVLEPVERVSTWVAFQSDGTVTSCDSLFAHLH GYVSGEDVAGQHITDLIPSVQLPPSGQHIPKNLKIQRSVGRAR DGTTFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISG LITLLPDGTIHGINHSFALTLFGYGKTELLGKNITFLIPGFYS YMDLAYNSSLQLPDLASCLDVGNESGCGERTLDPWQGQDPAEG GQDPRINVVLAGGHVVPRDEIRKLMESQDIFTGTQTELIAGGQ LLSCLSPQPAPGVDNVPEGSLPVHGEQALPKDQQITALGREEP VAIESPGQDLLGESRSEPVDVKPFASCEDSEAPVPAEDGGSDA GMCGLCQKAQLERMGVSGPSGSDLWAGAAVAKPQAKGQLAGGS LLMHCPCYGSEWGLWWRSQDLAPSPSGMAGLSFGTPTLDEPWL GVENDREELQTCLIKEQLSQLSLAGALDVPHAELVPTECQAVT APVSSCDLGGRDLCGGCTGSSSACYALATDLPGGLEAVEAQEV DVNSFSWNLKELFFSDQTDQTSSNCSCATSELRETPSSLAVGS DPDVGSLQEQGSCVLDDRELLLLTGTCVDLGQGRRFRESCVGH DPTEPLEVCLVSSEHYAASDRESPGHVPSTLDAGPEDTCPSAE EPRLNVQVTSTPVIVMRGAAGLQREIQEGAYSGSCYHRDGLRL SIQFEVRRVELQGPTPLFCCWLVKDLLHSQRDSAARTRLFLAS LPGSTHSTAAELTGPSLVEVLRARPWFEEPPKAVELEGLAACE GEYSQKYSTMSPLGSGAFGFVWTAVDKEKNKEVVVKFIKKEKV LEDCWIEDPKLGKVTLEIAILSRVEHANIIKVLDIFENQGFFQ LVMEKHGSGLDLFAFIDRHPRLDEPLASYIFRQVRAG\QSRLV SAVGYLRLKDIIHRDIKDENIVIAEDFTIKLIDFGSAAYLERG KLFYTFCGTIEYCAPEVLMGNPYRGPELEMWSLGVTLYTLVFE ENPFCELEETVEAAIHPPYLVSKELMSLVSGLLQPVPERRTTL EKLVTDPWVTQPVNLADYTWEEVFRVNKPESGVLSAASLEMGN RSLSDVAQAQELCGGPVPGEAPNGQGCLHPGDPRLLTS
383	1122	177	1365	PGTSAATCRFLSPPVISLSFTGLCISDLVVAVNGVWILVETFM LKGGNFFSKHVPWSYLVFLTIYGVELFLKVAGLGPVEYLSSGW NLFDFSVTVFAFLGLLALALNMEPFYFIVVLRPLQLLRLFKLK ERYRNVLDTMFELLPRMASLGLTLLIFYYSFAIVGMEFFCGIV FPNCCNTSTVADAYRWRNHTVGNRTVVEEGYYYLNNFDNILNS FVTLFELTVVNNWYIIMEGVTSQTSHWSRLYFMTFYIVTMVVM TIIVAFILEAFVFRMNYSRKNQDSEVDGGITLEKEISKEELVA VLELYREARGASSDVTRLLETLSQMERYQQHSMVFLGRRSRTK SDLSLKMYQEEIQEWYEEHAREQEQQRQLSSSAAPAAQQPPGS RQRSQTVT

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384	1123	1	986	LAGVGTQAPPRRPGGEMAAGQNGHEEWVGSAYLFVESSLDKVV LSDAYAHPQQKVAVYRALQAALAESGGSPDVLQMLKIHRSDPQ LIVQLRFCGRQPCGRFLRAYREGALRAALQRSLAAALAQHSVP LQL\DLRAGAERLEALLADEERCLSCILAQQPDRLRDEELAEL EDALRNLKCGSGARGGDGEVASAPLQPPVPSLSEVKPPPPPPP AQTFLFQGQPVVNRPLSLKDQQTFARSVGLKWRKVGRSLQRGC RALRDPALDSLAYEYEREGLYEQAFQLLRRFVQAEGRRATLQR LVEALEENELTSLAEDLLGLTDPNGGLA
385	1124	2409	399	SSKPKLKKRFSLRSVGRSVRGSVRGILQWRGTVDPPSSAGPLE TSSGPPVLGGNSNSNSSGGAGTVGRGLVSDGTSPGERWTHRFE RLRLSRGGGALKDGAGMVQREELLSFMGAEEAAPDPAGVGRGG GVAGPPSGGGGQPQWQKCRLLLRSEGEGGGGSRLEFFVPPKAS RPRLSIPCSSITDVRTTTALEMPDRENTFVVKVEGPSEYIMET VDAQHVKAWVSDIQECLSPGPCPATSPRPMTLPLAPGTSFLTR ENTDSLELSCLNHSESLPSQDLLLGPSESNDRLSQGAYGGLSD RPSASISPSSASIAASHFDSMELLPPELPPRIPIEEGPPAGTV HPLSAPYPPLDTPETATGSFLFQG\EPEGGEGDQPLSGYPWFH GMLSRLKAAQLVLTGGTGSHGVFLVRQSETRRGEYVLTFNFQG KAKHLRLSLNEEGQCRVQHLWFQSIFDMLEHFRVHPIPLESGG SSDVVLVSYVPSSQRQQGEQSRSAGEEVPVHPRSEAGSRLGAM RGCAREMDATPNASCTLMPFGASDC\EPTTSHDPPQPPEPPSW TDPPQPGEE\EASR\APGSGGQQAAAAAKERQEKEKAGG\GGV PEE\LVPVV*LVPVGELGEGHRPQAQEAQGRLGPGGDAGVPP\ MVQLQQSPLGG\DGEEGGHPR\AI\NNQYSFV
386	1125	2204	1042	FRAPVGTAARSPQVVIRRLPPGLTKEQLEEQLRPLPAHDYFEF FAADLSLYPHLYSRAYINFRNPDDILLFRDRFDGYIFLDSKDP EYKKFLETYCVEEEKTSANPETLLGEMEAKTRELIARRTTPLL EYIKNRKLEKQRIREEKREERRRRELEKKRLREEEKRRRREEE RCKKKETDKQKKIAEKEVRIKLLKKPEKGEEPTTEKPKERGEE IDTGGGKQESCAPGAVVKARPMEGSLEEPQETSHSGSDKEHRD VERSQEQESEAQRYHVDDGRRHRAHHEPERLSRRSEDEQRWGK GPGQDRGKKGSQDSGAPGEAMERLGRAQRCDDSPAPRKERLAN KDRPALQLYDPGARFRARECGGNRRICKAEGSGTGPEKREEAE
387	1126	176	800	GVWGVCVSGLLQVGSQRAQAWRAWSPMETPLTGTFLWPHIPQG LFFDDSYGFYPGQVLIGPAKIFSSVQWLSGVKPVLSTKSKFRV VVEEVQVVELKVTWITKSFCPGGTDSVSPP/PSVITQENLGRV KRLGCFDHAQR/HAWGALSVCLPSQGRASQDCLGMSRKKLRPG GGLYGQEGEAPVEEAGCADHVMLPRHPVFPGPFHGRPR

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388	1127	1	2017	FRDSSPCSAFEFHCLSGECIHSSWRCDGGPDCKDKSDEENCAV ATCRPDEFQCSDGNCIHGSRQCDREYDCKDMSDEVGCVNVTLC EGPNKFKCHSGECITLDKVCNMARDCRDWSDEPIKECGTNECL DNNGGCSHVCNDLKIGYECLCPDGFQLVAQRRCEDIDECQDPD TCSQLCVNLEGGYKCQCEEGFQLDPHTKACKAVGSIAYLFFTN RHEVRKMTLDRSEYTSLIPNLRNVVALDTEVASNRIYWSDLSQ RMICSTQLDRAHGVSSYDTVISRDIQAPDGLAVDWIHSNIYWT DSVLGTVSVADTKGVKRKTLFRENGSKPRAIVVDPVHGFMYWT DWGTPAKIKKGGLNGVDIYSLVTENIQWPNGITLDLLSGRLYW VDSKLHSISSIDVNGGNRKTILEDEKRLAHPFSLAVFEDKVFW TDIINEAIFSANRLTGSDVNLLAENLLSPEDMVLFHNLTQPRG VNWCERTTLSNGGCQYLCLPAPQINPHSPKFTCACPDGMLLAR DMRSCLTEG\EAAVATQETSTVRLKVSSTAVRTQHTTTRPVPD TSRLPGATPGLTTVEIVTMSHQALGDVAG\RGN\EKKPSSVRA LSIVLPIV\LLVFLCLGVFLLWKNWRLKNINSINFDNPVYQKT TEDEVHICHNQDGYSYPSRQMVSLEDDVA
389	1128	2299	1148	RIPGLGPPGSPPPPPHVRGMPGCPCPGCGMAGPRLLFLTALAL ELLGRAGGSQPALRSRGTATACRLDNKESESWGALLSGERLDT WICSLLGSLMVGLSGVFPLLVIPLEMGTMLRSEAGAWRLKQLL SFALGGLLGNVFLHLLPEAWAYTCSASPGGEGQSLQQQQQLGL WVIAGILTFLALEKMFLDSKEEGTSQAPNKDPTAAAAALNGGH CLAQPAAEPGLGAVVRSIKVSGYLNLLANTIDNFTHGLAVAAS FLVSKKIGLLTTMAILLHEIPHEVGDFAILLRAGFDRWSAAKL QLSTALGGLLGAGFAICTQSPKGVEETAAWVLPFTSGGFLYIA LVNVLPDLLEEEDPWRSLQQLLLLCAGIVVMVLFSLFVD
390	1129	1	523	GKVSAGQAGADRTLRRAPEPRFSQEPTGNSAYPQLRPFLDPQG RDLKPSALVPPTRSHTGRRPWLHTQPLPGPQGRAWGPTC/TPA CVDRVLESEEGRREYLAFPTSKSSGQKGRKELLKGNGRRIDYM LHAEEGLCPDWKAEVEEFSFITQLSGLTDHLPVAMRLMVSSGE EEA
391	1130	1459	765	PCGGIRLSASEAATLFGYLVVPAGGGGTFLGGFFVNKLRLRGS AVIKFCLFCTVVSLLGILVFSLHCPSVPMAGVTASYGGSLLPE GHLNLTAPCNAACSCQPEHYSPVCGSDGLMYFSLCHAGCPAAT ETNVDGQKVSGAAAYRPCPPLDPGKGPPCLPLVIGAIVGLPRC TETVAVSLRIFPLVLAM\HCREMHFNLSEKAPPSGFHIRCNFL YIPQQHSCTNGNSTMCP
392	1131	1668	962	LLRKVGAPGGARGVIRLLDWFERPDGFLLVLERPEPA\QD\LF DFITERGALDEPLARRF\FAQVLAAVRHCHSCGVVHRDIKDEN LLVDLRSGELKLIDFGSGALLKDTVYTDFDGTRVYSPPEWIRY HRYHGRSATVWSLGVLLYDMVCGDIPFEQDEEILRGRLLFRRR VSPECQQLIRWCLSLRPSERPSLDQIAAHPWMLGADGGAPESC DLRLCTLDPDDVASTTSSSESL

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393	1132	3	817	GKNSQKASPVDDEQLSVCLSGFLDEVMKKYGSLVPLSEKEVLG RLKDVFNEDFSNRKPFINREITNYRARHQKCNFRIFYNKHMLD MDDLATLDGQNWLNDQVINMYGELIMDAVPDKVHFFNSFFHRQ LVTKGYNGVKRWTKKVDLFKKSLLLIPIHLEVHWSLITVTLSN RIISFYDSQGIHFKFCVENIRKYLLTEAREKNR\LNLQGWQTA VTKCIPQQKNDSDCGVFVLQYCKCLAL\KQPFQFSQEDMPRVR KRIYKELCECRLMD
394	1133	1252	628	PPGG*QGSAAKHR/FP/KGYRHPALEARLGRRRTVQEARALLR CRRAGISAPVVFFVDYASNCLYMEEIEGSVTVRDYIQSTMETE K\TPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLE QLNIVLIDFGLSFISALPEDKGVDLYVLEKAFLSTHPNTETVF EAFLKSYSTSSKKARPVLKKLDEVRLRGKKRSMVG
395	1134	2	1595	RACVFRPEDMMQGEAHPSASLIDRTIKMRKETEARKVVLAWGL LNVSMAGMIYTEMTGKLISSYYNVTYWPLWYIELALASLFSLN ALFDFWRYFKYTVAPTSLVVSPGQQTLLGLKTAVVQTTPPHDL AATQIPPAPPSPSIQGQSVLSYSPSRSPSTSPKFTTSCMTGYS PQLQGLSSGGSGSYSPGVTYSPVSGYNKLASFSPSPPSPYPTT VGPVESSGLRSRYRSSPTVYNSPTDKEDYMTDLRTLDTFLRSE EEKQHRVKLGSPDSTSPSSSPTFWNYSRSMGDYAQTLKKFQYQ LACRSQAPCANKDEADLSSKQAAEEVWARVAMNRQLLDHMDSW TAKFRNWINETILVPLVQEIESVSTQMRRMGCPELQIGEASIT SLKQAALVKAPLIPTLNTIVQYLDLTPNQEYLFERIKELSQGG CMSSFRWNRGGDFKGRKWDTDLPTDSAIIMHVFCTYLDSRLPP HPKYPDGKTFTSQHFVQTPNKPDVTNENVFCIYQSAINPPHYE LIYQRHVYIPAKGQK
396	1135	16	1542	SSAVEFINRNNSVVQVLLAAGADPNLGDDFSSVYKTAKEQGIH SLEVLITREDDFNNRLNNRASFKGCTALHYAVLADDYRTVKEL LDGGANPLQRNEMGHTPLDYAREGEVMKLLRTSEAKYQEKQRK REAEERRRFPLEQRLKEHIIGQESAIATVGAAIRRKENGWYDE EHPLVFLFLGSSGIGKTELAKQTAKYMHKDAKKGFIRLDMSEF QERHEVAKFIGSPPGYVGHEEGGQLTKKLKQCPNAVVLFDEVD KAHPDVLTIMLQLFDEGRLTDGKGKTIDCKDAIFIMTSNVASD EIAQHALQLRQEALEMSRNRIAENLGDVQISDKITISKNFKEN VIRPILKAHFRRDEFLGRINEIVYFLPFCHSELIQLVNKELNF WAKRAKQRHNITLLWDREVADVLVDGYNVHYGARSIKHEVERR VGNQLAAAYEQDLLP\GGCTLRITVEDSDKQLLKSPELPSPQA EKRLPKLRLEIIDKDSKTRRLDIRAPLHPEKVCNTI
397	1136	1848	1602	SSCDRERHGSLGMMSGSFILCLALVTRWSPQASSVPLAVYESK TRKSYRSQRDRDGKDRSQGMGLSLLVETRKLLLSANQG

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398	1137	1497	717	HTPMA/FFL/SFLSTSET/VYTFVILPKMLINLLSVARTISFN CCALQMFFFLGFAITNCLLLGVMGYDRYAAICHPLHYPTLMSW QVCGKLAAACAIGGFLASLTVVNLVFSLPFCSTNKVNHYFCDI SAVILLACTNTDVNGFVIFICGVLVLVVPFLFICVSYFCILRT ILKIPSAEGRRKAFSTCASHLSVVIVHYGCASFIYLRPTANYV SNKDRLVTVTYTIVTPLLNPMVYSLRNKDVQLAIRKVLGKKGS LKLYN
399	1138	2	1185	RPPAATRYPREKLKSMTSRDNYKAGSREAA\AAAAAAVAAAAA AAAAAEPYPVSGAKRKYLEDSDPERSDYEEQQLQEEEEARKVK SGIRQMRLFSQDECAKIEARIDEVVSRAEKGLYNEHTVDRAPL RNKYFFGEGYTYGAQLQKRGPGQERLYPPGDVDEIPEWVHQLV IQKLVEHRVIPEGFVNSAVINDYQPGGCIVSHVDPIHIFERPI VSVSFFSDSALCFGCKFQFKPIRVSEPVLSLPVRRGSVTVLSG YAADEITHCIRPQDIKERRAVIILRKTRLDAPRLETKSLSSSV LPPSYASDRLSGNNRDPALKPKRSHRKADPDAAHRPRILEMDK EENRRSVLLPTHRRRGSFSSENYWRKSYESSEDCSEAAGSPAR KVKMRRH
400	1139	60	1699	VTWHFYFCSDHKNGHYIIPQMADRSRQKCMSQSLDLSELAKAA KKKLQALSNRLFEELAMDVYDEVDRRENDAVWLATQNHSTLVT ERSAVPFLPVNPEYSATRNQGRQKLARFNAREFATLIIDILSE AKRRQQGKSLSSPTDNLELSLRSQSDLDDQHDYDSVASDEDTD QEPLRSTGATRSNRARSMDSSDLSDGAVT\LQEYLELKKALAT SEAKVQQLMKVNSSLSDEL\RRLQREHFAPI\IHKLQAENLQL RQPPGPVPTPPLPSERAEHTPMAPGGSTHRRDRQAFSMYEPGS ALKPFGGPPGDELTTRLQPFHSTELEDDAIYSVHVPAGLYRIR KGVSASAVPFTPSSPLLSCSQEGSRHTSKLSRHGSGADSDYEN TQSGDPLLGLEGKRFLELGKEEDFHPELESLDGDLDPGLPSTE DVILKTEQVTKNIQELLRAAQEFKHDSFVPCSEKIHLAVTEMA SLFPKRPALEPVRSSLRLLNASAYRLQSECRKTVPPEPGAPVD FQLLTQQVIQCAYDIAKAAKQLVTITTREKKQ

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401	1140	1	1863	RYLSYGSGPKRFPLVDVLQYALEFASSKPVCTSPVDDIDASSP PSGSIPSQTLPSTTEQQGALSSELPSTSPSSVAAISSRSVIHK PFTQSRIPPDLPMHPAPRHITEEELSVLESCLHRWRTEIENDT RDLQESISRIHRTIELMYSDKSMIQVPYRLHAVLVHEGQANAG HYWAYIFDHRESRWMKYNDIAVTKSSWEELVRDSFGGYRNASA YCLMYINDKAQFLIQEEFN/K/ETGQPLVGIETLPPDLRDFVE EDNQRFEKELEEWDAQLAQKALQEKLLASQKLRESETSVTTAQ AAGDPKYLEQPSRSDFSKHLKEETIQIITKASHEHEDKSPETV LQSAIKLEYARLVKLAQEDTPPETDYRLHHVVVYFIQNQAPKK IIEKTLLEQFGDRNLSFDERCHNIMKVAQAKLEMIKPEEVNLE EYEEWHQDYRKFRETTMYLIIGLENFQRESYIDSLLFLICAYQ NNKELLSKGLYRGHDEELISHYRRECLLKLNEQAAELFESGED REVNNGLIIMNEFIVPFLPLLLVDEMEEKDILAVEDMRNRWCS YLGQEMEPHLQEKLTDFLPKLLDCSMEIKSFHEPPKLPSYSTH ELCERFARIMLSLSRTPADGR
402	1141	1	465	AQVYVRMDSFDEDLARPSGLLAQERKLCRDLVHSNKKEQEFRS IFQHIQSAQSQRSPSELFAQHM\VPIVHHVKEHHFGSSGMTLH ERFT\KYLKRG\TEQEAAKNKKSPEIHRRIDISPSTFRKHGLA HDEMKSPREPGYKDGHNSKNELQRVNFY
403	1142	2	369	TYTFCFSLMI\ILLTIIQGLILEAFGELRDQLDQVKEDMETKC FICGIGNDYFDTVPHGFETHTLQEHNLANYLFFLMYLINKDET EHTGQESYVWKMYQERCWEFFPAGDCFRKQYEDQLN
404	1143	3115	557	FRRKGGGGPKDFGAGLKYNSRHEKVNGLEEGVEFLPVNNVKKV EKHGPGRWVVLAAVLIGLLLVLLGIGFLVWHLQYRDVRVQKVF NGYMRITNENFVDAYENSNSTEFVSLASKVKDALKLLYSGVPF LGPYHKESAVTAFSEGSVIAYYWSEFSIPQHLVEEAERVMAEE RVVMLPPRARSLKSFVVTSVVAFPTDSKTVQRTQDNSCSFGLH ARGVELMRFTTPGFPDSPYPAHARCQWALRGDADSVLSLTFRS FDLASCDERGRHLV\TVYNT\LSPMEPHA\LVQLCGTYPPSYN LTFHS\S\QNVLLITLITNTERRHPG\FEATFFQLPRMSSCGG RLRKAQGTFNSPYYPGHYPPNIDCTWNIEVPNNQHVKVRFKFF YLLEPGVPAGTCPKDYVEINGEKYCGERSQFVVTSNSNKITVR FHSDQSYTDTGFLAEYLSYDSSDPCPGQFTCRTGRCIRKELRC DGWADCTDHSDELNCSCDAGHQFTCKNKFCKPLFWVCDSLNDC GDNSDEQGCSCP\AQTFRCSNGKCLSKSQQCNGKDDCGDGSDE ASCPKVNVVTCTKHTYRCLNGLCLSKGNPECDGKEDCSDGSDE KDCDCGLRSFTRQARVVGGTDADEGEWPWQVSLHALGQGHICG ASLISPNWLVSAAHCYIDDRGFRYSDPTQWTAFLGLHDQSQRS APGVQERRLKRIISHPFFNDFTFDYDIALLELEKPAEYSSMVR PICLPDASHVFPAGKAIWVTGWGHTQYGGTGALILQKGEIRVI NQTTCENLLPQQITPRMMCVGFLSGGVDSCQGDSGGPLSSVEA DGRIFQAGVVSWGDGCAQRNKPGVYTRLPLFRDWIKENTGV

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405	1144	1	424	RHEEDLGNLWENTRFTDCSFFVRGQEFKAHKSVLAARSPVFNA MFEHEMEESKKNRVEINDLDPEVFKEMMRFIYTGRAPNLDKMA DNLLAAADKYALERLKVMCEKALCSNLSVENVADTLVLADLHS \AEQLKAQAIDFINRCSVLRQLGCKDGKNWNSNQATDIMETSG GKSMIQSHPHLVAEAFRALASAQGPQFGIPRKRLKQS*NLGNL WENTRFTDCSFFVRGQEFKAHKSVLAARSPVFNAMFEHEMEES KKNRVEINDLDPEVFKEMMRFIYTGRAPNLDKMADNLLAAADK YALERLKVMCEKALCSNLSVENVADTLVLADLHSGRTVESTSH RLY
406	1145	1	1021	QRGGIPGKFQEDSGSVDWALGPFWGIFQADFGCMRFYLSAQTS DPVLRM*WGPSPISHPTSLCPGGGGAGQTTGSLCLGQQCCPLS CPNIPSRHKRWRL*AALVAGSRGSCTLRS*R*RTPLPVTRNLP R/CHLHLHPTGDLRVHVHQHCLLHGHVPPGAALLQCGGCDLRG EAAGLLFLGHACLRGSVNLRRDQWLPV\PYSRLCFSGAREGHL PSLLAMIHVRHCTPIPALLVC\PIKVNLLIPVAYLVFWAFLLV FSFISEHMVCGVGVIIILTGVPIFFLGVFWRSKPKCVHRLTES MTHWGQELCFVVYPQDAPEEEENGPCPPSLLPATDKPSKPQ
407	1146	2	1280	AAALVAEYLALLEDHRHLPVGCVSFQNISSNVLEESAISDDIL SPDEEGFCSGKHFTELGLVGLLEQAAGYFTMGGLYEAVNEVYK NLIPILEAHRDYKKLAAVHGKLQEAFTKIMHQSSGWERVFGTY FRVGFYGAHFGDLDEQEFVYKEPSITKLAEISHRLEEFYTERF GDDVVEIIKDSNPVDKSKLDSQKAYIQITYVEPYFDTYELKDR VTYFDRNYGLRTFLFCTPFTPDGRAHGELPEQHKRKTLLSTDH AFPYIKTRIRVCHREETVLTP\VEVAIEDMQKKTRELAFATEQ DPPDAKMLQMVLQGSVGPTVNQGPLEVAQVFLAEIPEDPKLFR HHNKLRLCFKDF*KKCEDALRKNKALIGPDQKEYHRELERNY CRLREALQPLLTQRLPQLMAPTPPGLRNSLNRASFRKADL
408	1147	55	651	GEGQQWQSTPLSPLQPTVADFLNLAWWTSAAAW*VLSGRWVEK VLPGREGSEEK*GMASSSADHLHSAPRALQ\SLFQQLLYGLIY HSWFQAGR*GFGGASSSPGPQSELRRLHGEGGVYD*GRPETLP GSVGGAEALWALADPAEAEGSPETRESSCVMKQTQYYFGSVNA SYNAIIDCGNCSRCWQWGGTRGQGRNL
409	1148	1855	904	VAGIPACFDN/FTEALAETACRQMGYSSKPTFRAVEIGPDQDL DVVEITENSQELRMRNSSGPCLSGSLVSLHCLACGESLKTPRV VGGEEASVDSWPWQVSIQYDKQHVCGGSILDPHWVLTAAHCFR KHTDVFNWKVRAGSDKLGSFPSLAVAKIIIIEFNPMYPKDNDI ALMKLQFPLTFSGTVRPICLPFFDEELTPATPLWIIGWGFTKQ NGGKMSDILLQASVQVIDSTRCNADDAYQGEVTEKMMCAGIPE GGVDTCQGDSGGPLMYQSDQWHVVGIVSWGYGCGGPSTPGVYT KVSAYLNWIYNVWKAEL

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410	1149	3	964	TISTVRWNSRIGMVLGVAIQKRAV\PGLY\APEEAYARADKEA PRPCHKGSWCSSNQLCRECQAFMAHTMPKLKAFSMSSAYNAYR AVYAVAHGLHQLLGCASGACSRGRVYPWQLLEQIHKVHFLLHK DTVAFNDNRDPLSSYNIIAWDWNGPKWTFTVLGSSTWSPVQLN INETKIQWHGKDNQVPKSVCSSDCLEGHQRVVTGFHHCCFECV PCGAGTFLNKS/SYLGKDLPENYNEAKCVTFSLLFNFVSWIAF FTTASVYDGKYLPAANMMAGLSSLSSGFGGYFLPKCYVILCRP DLNSTEHFQASIQDYTRRCGST
411	1150	2	1378	VARGAFHPKMGPSFPSPKPGSERLSFVSAKQSTGQDTEAELQD ATLALHGLTVEDEGNYTCEFATFPKGSVRGMTWLRVIAKPKNQ AEAQKVTFSQDPTTVALCISKEGRPPARISWLSSLDWEAKETQ VSGTLAGTVTVTSRFTLVPSGRADGVTVTCKVEHESFEEPALI PVTLSVRYPPEVSISGYDDNWYLGRTDATLSCDVRSNPEPTGY DWSTTSGTFPTSAVAQGSQLVIHAVDSLFNTTFVCTVTNAVGM GRAEQVIFVRETPNTAGAGATGGIIGGIIAAIIATADA\TGIL ICRQQRKEQTLQGAEEDEDLEGPPSYKPPTPKAKLEAQEMPSQ LFTLGASEHSPLKTPYFDAGASCTEQEMPRYHELPTLEERSGP LHPGATSLGSPIPVPPGPPAVEDVSLDLEDEEGEEEEEYLDKI NPIYDALSYSSPSDSYQGKGFVMSRAMYV
412	1151	1	1828	GTRLREDKNHNMYVAGCTEVEVKSTEEAFEVFWRGQKKRRIAN THLNRESSRSHSVFNIKLVQAPLDADGDNVLQEKEQITISQLS LVDLAGSERTNRTRAEGNRLREAGNINQSLMTLRTCMDVLREN QMYGTNKMVPYRDSKLTHLFKNYFDGEGKVRMIVCVNPKAEDY EENLQVMRFAEVTQEVEVARPVDKAICGLTPGRRYRNQPRGP\ IGNEPLVTDVVLQSFPPLPSCEILDINDEQTLPRLIEALEKRH NLRQMMIDEFNKQSNAFKALLQEFDNAVLSKENHMQGKLNEKE KMISGQKLEIERLEKKNKTLEYKIEILEKTTTIYEEDKRNLQQ ELETQNQKLQRQFSDKRRLEARLQGMVTETTMKWEKECERRVA AKQLEMQNKLWVKDEKLKQLKAIVTEPKTEKPERPSRERDREK VTQRSVSPSPVPLLFQPDQNAPPIRLRHRRSRSAGDRWVDHKP ASNMQTETVMQPHVPHAITVSVANEKALAKCEKYMLTHQELAS DGEIETKLIKGDIYKTRGGGQSVQFTDIETLKQESPNGSRKRR SSTVAPAQPDGAESEWTDVETRCSVAVEMRAGSQLGPGYQHHA QPKRKKP
413	1152	1	336	PFSSSSVSSKGSDPFGTLDPFGSGSFNSAEGFADFSQMS/KGK STPVSQLGSADFPEAPDPFQPLGADSGDPFQSKKGFGDPFSGK DPFVPSSAAKPSKASASGFADFTSVS

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414	1153	1	1334	MSLMVVSMACVGLFLVQRAGPHMGGQDKPFLSAWPSAVVPRGG HVTLRCHYRHRFNNFMLYKEDRIHIPIFHGRIFQESFNMSPVT TAHAGNYTCRGSHPHSPTGWSAPSNPVVIMVTGNHRKPSLLAH PGPLVKSGERVILQCWSDIMFEHFFLHKEGISKDPSRLVGQIH DGVSKANFSIGPMMQDLAGTYRCYGSVTHSPYQLSAPSDPLDI VITGLYEKPSLSAQPGPTVLAGESVTLSCSSRSSYDMYHLSRE GEAHERRFSAGPKVNGTFQADFPLGPATHGGTYRCFGSFRDSP YEWSNSSDPLLVSVTGNPSNSWPSPTEPSSETGNPRHLHVLIG TSVVIILFILLLFFLLHRWCSN\KKNAAVMDQESAGNRTANSE DSDEQDPQEVTYTQLNHCVFTQRKITRPSQRPKTPPTDIIVYT ELPNAESRSKVVSCP
415	1154	1	1570	MSLRVHTLPTLLGAVVRPGCRELLCLLMITVTVGPGASGVCPT ACICATDIVSCTNKNLSKVPGNLFRLIKRLDLSYNRIGLLDSE WIPVSFAKLNTLILRHNNITSISTGSFSTTPNLKCLDLSSNKL KT\VKNAVFQELKVLEVLLLYNNHISYLDPSAFGGLSQLQKLY LSGNFLTQFPMDLYVGRFKLAELMFLDVSYNRIPSMPMHHINL VPGKQLRGIYLHGNPFVCD\CSLVSLLVFWYRRHFSSVMDFKN DYTCRLWSDSRHSRQVLLLQDSFMNCSDSIINGSFRALGFIHE AQVGERLMVHCDSKTGNANTDFIWVGPDNRLLEPDKEMENFYV FHNGSLVIESPRFEDAGVYSCIAMNKQRLLNETVDVTINVSNF TVSRSHAHEAFNTAFTTLAACVASIVLVLLYLYLTPCPCKCKT KRQKNMLHQSNAHSSILSPGPASDASADERKAGAGKRVVFLEP LKDTAAGQNGKVRLFPSEAVIAEGILKSTRGKSDSDSVNSVFS DTPFVAST
416	1155	2	1928	ASDFIRSLDHCGYLSLEGVFSHKFDFELQDVSSVNEDVLLTTG LLCKYTAQRFKPKYKFFHKSFQEYTAGRRLSSLLTSHEPEEVT KGNGYLQKMVSISDITSTYSSLLRYTCGSSVEATRAVMKHLAA VYQHGCLLGLSIAKRPLWRQESLQSVKNTTEQEILKAININSF VECGIHLYQESTSKSALSQEFEAFFQGKSLYINSGNIPDYLFD FFEHLPNCASALDFIKLGFYGGAMASWEKAAEDTGGIHMEEAP ETYIPSRAVSLFFNWKQEFRTLEVTLRDFSKLNKQDIRYLGKI FSSATSLRLQIKRCAGVAGSLSLVLSTCKNIYSLMVEASPLTI EDERHITSVTNLKTLSIHDLQNQRLPGGLTDSLGNLKNLTKLI MDNIKMNEEDAIKLAEGLKNLKKMCLFHLTHLSDIGEGMDYIV KSLSSEPCDLEEIQLVSCCLSANAVKILAQNLHNLVKLSILDL SENYLEKDGNEALHELIDRMNVLEQLTALMLPWGCDVQGSLSS LLKHLEEVPQLVKLGLKNWRLTDTEIRILGAFFGKNPLKNFQQ LNLAGNRVSSDGWLAFMGVFENLKQLVFFDFSTKEFLPDPALV RKLSQVLSKLTFLQEARLVGWQFDDDDLSVITGAFKLVTA
417	1156	342	718	ASDRKVAMTCDCFWFRTMLDQHASCMEVGTERERQAG\GLVMF DPSGFPTGEKVLQDDEFTCDLFRFLQLLCEGHNSGL*VPGTSD DTKA*IMFSSQ**QEPVSSNYASF*RQQIILEHGSALGSG

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418	1157	1	135	EITHIVGETAAFLCPRLRLRRGGKDGSPKPGFLASVIPVDRRP GE*DITHIVGETAAFLCPRLRLRRGGKDGSPKPGFLASVIPVD RRPGE
419	1158	173	943	SKFIFYVDSQSMIFFFQTPTRHKVLIMEFCPCGSLYTVLEEPS NAYGLPESEFLIVLRDVVGGMNHLRENGIVHRDIKPGNIMRVI GEDGQSVYKLTDFGAARELEDDEQFVSLYGTEEYLHPDMYERA VLRKDHQ\KKYGAT\VDLW\SIGVTFYQGKPTGS\LAI*HPFE GASVRNKASDGIKIITGKGLLGAIS\GVQKSKKNG\PI\DWEW EDMPVSCSPSSGVLRVPNLPPVLA\NILESRSRKKCWGF*PSF LQEN
420	1159	987	500	GSTISCERSLRSLWTAHWALPEMDSRIPYDDYPVVFLPAYENP PAWIPPHERVHHPDYNNELTQFLPRTITLKKPPGAQLGFNIRG GKASQLGIFISKVIPDSDAHRAGLQEGDQVLAVNDVDFQDIEH SKAVEILKTAREISMRVRFFPYNYHRQKERTVH
421	1160	3	890	HEQVSALHRRIKAIVEVAAMCGVNIICFQEAWTMPFAFCTREK LPWTEFAESAEDGPTTRFCQKLAKNHDMVVVSPILERDSEHGD VLWNTAVVISNSGAVLGKTRKNHIPRVGDFNESTYYMEGNLGH PVFQTQFGRIAVNICYGRHHPLNWLMYSINGAEIIFNPSATIG ALSESLWPIEARNAAIANHCFTCAINRVGTEHFPNEFTSGDGK KAHQDFGYFYGSSYVAAPDSSRTPGLSRSRDGLLVAKLDLNLC QQVNDVWNFKMTGRYEMYARELAEAVKSNYSPTIVKE

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422	1161	5214	352	MAKSGGCGAGAGVGGGNGALTWVNNAAKKEESETANKNDSSKK LSVERVYQKKTQLEHILLRPDTYIGSVEPLTQFMWVYDEDVGM NCREVTFVPGLYKIFDEILVNAADNKQRDKNMTCIKVSIDPES NIISIWNNGKGIPVVEHKVEKVYVPALIFGQLLTSSNYDDDEK KVTGGRNGYGAKLCNIFSTKFTVETACKEYKHSFKQTWMNNMM KTSEAKIKHFDGEDYTCITFQPDLSKFKMEKLDKDIVALMTRR AYDLAGSCRGVKVMFNGKKLPVNGFRSYVDLYVKDKLDETGVA LKVIHELANERWDVCLTLSEKGFQQISFVNSIATTKGGRHVDY VVDQVVGKLIEVVKKKNKAGVSVKPFQVKNHIWVFINCLIENP TFDSQTKENMTLQPKSFGSKCQLSEKFFKAASNCGIVESILNW VKFKAQTQLNKKCSSVKYSKIKGIPKLDDANDAGGKHSLECTL ILTEGDSAKSLAVSGLGVIGRDRYGVFPLRGKILNVREASHKQ IMENAEINNIIKIVGLQYKKSYDDAQSLKTLRYGKIMIMTDQD QDGSHIKGLLINFIHHNWPSLLKHGFLEEFITPIVKASKNKQE LSFYSIPEFDEWKKHIENQKAWKIKYYKGLGTSTAKEAKEYFA DMERHRILFRYAGPEDDAAITLAFSKKKIDDRKEWLTNFMEDR RQRRLHGLPEQFLYGTATKHLTYNDFINKELILFSNSDNERSI PSLVDGFKPGQRKVLFTCFKRNDKREVKVAQLAGSVAEMSAYH HGEQALMMTIVNLAQNFVGSNNINLLQPIGQFGTRLHGGKDAA SPRYIFTMLSTLARLLFPAVDDNLLKFLYDDNQRVEPEWYIPI IPMVLINGAEGIGTGWACKLPNYDAREIVNNVRRMLDGLDPHP MLPNYKNFKGTIQELGQNQYAVSGEIFVVDRNTVEITELPVRT WTQVYKEQVLEPMLNGTDKTPALISDYKEYHTDTTVKFVVKMT EEKLAQAEAAGLHKVFKLQTTLTCNSMVLFDHMGCLKKYETVQ DILKEFFDLRLSYYGLRKEWLVGMLGAEFTKLNNQARFILEKI QGKITI*NRSKKDLIQMLVQRGYESDPVKAWKEAQEKAAEEDE TQNQHDDSSSDSGTPSGPDFNYILNMSLWSLTKEKVEELIKQR DAKGREVNDLKRKSPSDLWKEDLAAFVEELDKVESQEREDVLA GMSGKAIKGKVGKPKVKKLQLEETMPSPYGRRIIPEITAMKAD ASKKLLKKKKGDLDTAAVKVEFDEEFSGAPVEGAGEEALTPSV PINKGPKPKREKKEPGTRVRKTPTSSGKPSAKKVKKRNPWSDD ESKSESDLEETEPVVIPRDSLLRRAAAERPKYTFDFSEEEDDD ADDDDDDNNDLEELKVKASPITNDGEDEFVPSDGLDKDEYTFS PGKSKATPEKSLHDKKSQDFGNLFSFPSYSQKSEDDSAKFDSN EEDSASVFSPSFGLKQTDKVPSKTVAAKKGKPSSDTVPKPKRA PKQKKVVEAVNSDSDSEFGIPKKTTTPKGKGRGAKKRKASGSE NEGDYNPGRKTSKTTSKKPKKTSFDQDSDVDIFPSDFPTEPPS LPRTGRARKEVKYFAESDEEEDDVDFAMFN
423	1162	1	219	KGCLAASFNCIFLYTGELYPTMIR*VEA*WENDSLFLGKDILL CTGQTPELNQVHPSPKAPPNTHHCKAHSSH

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424	1163	1454	446	ENSFECKDCGKAFSRGYQLSHHQKIHTGEKPYECKECKKAFRW GNQLTQHQKIHTGEKPYECKDCGKAFRWGSSLVIHKRIHTGEK PYECKDCGKAFRRGDELTQHQRFHTGEKDYECKDCGKTFSRVY KLIQHKRIHSGEKPYECKDCGKAFICGSSLIQHKRIHTGEKPY ECQECGKAFTRVNYLTQHQKIHTGEKPHECKECGKAFRWGSSL VKHERIHTGEKPYKCTECGKAFNCGYHLTQHERIHTGETPYKC KECGKAFIYGSSLVKHERIHTGVKPYGCTECGKSFSHGHQLTQ HQKTHSGAKSYECKECGKACNHLNHLREHQRIHNS
425	1164	826	407	HQYLDDLYPLHVMTILLKSHFFTMLKRPVGSSSFASLPFYHQS ILLRKNQMKRKKTQQDLTHINWTLQAVSIQTCIWLQKKPSSYF HQLPNQVL*PENSGPESCLYDLAAVVVHHGSG
426	1165	464	29	XLDPDTLPAVATLLMDVMFYSNGVKDPMATGDDCGHIRFFSFS LIEGYISLVMDVQTQQRFPSNLLFTSASGELWKMVRIGGQPLG FGPVWESGPTGPTSPLILPVTPSSSHRQAASQVTTTKQGQWLC LKRPSARSPDHTACLG*
427	1166	649	901	EAPLTSVCFSLERRFGSSSNTTSFGTLASQNAPTFGSLSQQTS GFGTQSSGFSGFGSGTGGFSFGSNNS*VSPFLSLTLIKSIK
428	1167	3	340	EEPQGSPIWVWLAGSLTSVSCFLPFQRMRIKPHQGQYIGEMSF LQHHKGECRPQKD*ARQENPCGPCSERRKHLLGQDPKTCKCSC KNTDSRCKARPLELNERTCRCDKPRR
429	1168	355	1312	TLWAGPGLCPQSHSSSSVPAPWEPHVERALRTDRNQGQRPLLS ASWAPAPARPLFLTSPVLLPKSRAIPAARDPS*AGIFCLLEMA GGQASVVIIGSAGVLGCRWGSSGKSHSLSPSRKGNLHLLSQEP QTTVVHNATDGIKGSTESCNTTTEDEDLKVRKQEIIKITEQLI EAINNGDFEAYTKICDPGLTSFEPEALGNLVEGMDFHKFYFEN REWVRAADILLPAPLPLCLCLLLTFSSQLPTFPLFDLRAALLL CMLVPLCPDGCRQAPLKALLLSSKCHSFCSCFVAVPVTTIKLT YFLPGAVAYACNPNTLGG
430	1169	439	728	ERAGAGGAAACRAGTRSGATSRTPWPLHRQLSMMLMLAQSNPQ LFALMGTRAGIARELERVEQQSRLEQLSAAELQSRNQGHWADW LQAYRARLGQ
431	1170	3	440	NGTLFIMVMHIKDLVSDYKE*WL*RKPLPW*EALLLRDCFFF* VTENGADPNPYVKTYLLPDNHKTSKRKTKISRKTRNPTFNEML VYSGYSKETLRQRELQLSVLSAESLRENFFLGGVTLPLKDFNL SKETVKWYQLTAATYL

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432	1171	433	1824	LHRIMQLAVVVSQVLENGSSVLVCLEEGWDITAQVTSLVQLLS DPFYRTLEGFQMLVEKEWLSFGHKFSQRSSLTLNCQGSGFAPV FLQFLDCVHQVHNQYPTEFEFNLYYLKFLAFHYVSNRFKTFLL DSDYERLEHGTLFDDKGEKHAKKGVCIWECIDRMHKRSPIFFN YLYSPLEIEALKPNVNVSSLKKWDYYIEETLSTGPSYDWMMLT PKHFPSEDSDLAGEAGPRSQRRTVWPCYDDVSCTQPDALTSLF SEIEKLEHKLNQAPEKWQQLWERVTVDLKEEPRTDRSQRHLSR SPGIVSTNLPSYQKRSLLHLPDSSMGEEQNSSISPSNGVERRA ATLYSQYTSKNDENRSFEGTLYKRGALLKGWKPRWFVLDVTKH QLRYYDSGEDTSCKGHIDLAEVEMVIPAGPSMGAPKHTSDKAF FDLKTSKRVYNFCAQDGQSAQQWMDKIQSCISDA
433	1172	1714	946	EVEGPRRVSPAPETLGMEESVVRPSVFVVDGQTDIPFTRLGRS HRRQSCSVARVGLGLLLLLMGAGLAVQGWFLLQLHWRLGEMVT RLPDGPAGSWEQLIQERRSHEVNPAAHLTGANSSLTGSGGPLL WETQLGLAFLRGLSYHDGALVVTKAGYYYIYSKVQLGGVGCPL GLASTITHGLYKRTPRYPEELELLVSQQSPCGRATSSSRVWWD SSFLGGVVHLEAGEEVVVRVLDERLVRLRDGTRSYFGAFMV
434	1173	16	367	QSAELGPRRREGSRRPSCTKASKPWRRRPGGPTSGLG*GPLSP GPYQCRPSLPAQLYPQSLMAAATLRTPTQVSAASSRPHTPSPT HVLKPSVRGACSSPRCPGSGTLRRSWVGPFF
435	1174	27	1139	LWWPPLSRHAAHRQWPGPTAPRGLGHKVKGRGASPAAMWSCSW FNGTGLVEELPACQDLQLGLSLLSLLGLVVGVPVGLCYNALLV LANLHSKASMTMPDVYFVNMAVAGLVLSALAPVHLLGPPSSRW ALWSVGGEVHVALQIPFNVSSLVAMYSTALLSLDHYIERALPR TYMASVYNTRHVCGFVWGGALLTSFSSLLFYICSHVSTRALEC AKMQNAEAADATLVFIGYVVPALATLYALVLLSRVRREDTPLD RDTGRLEPSAHRLLVATVCTQFGLWTPHYLILLGHTVIISRGK PVDAHYLGLLHFVKDFSKLLAFSSSFVTPLLYRYMNQSFPSKL QRLMKKLPCGDRHCSPDHMGVQQVLA
436	1175	322	756	SESELFTLMPSLPTTNCVHSLQMIPPLSPAPNQELVLGLCYMS YLAFLYMTFDFCCLYFSTVYAPSFKYICVHTDTHICVCVCIYL SSVVSKSSAEADGVLQPRRHPASLLIVFATSISESSLLIFSFQ KTEAKLIVFAVSLAAK
437	1176	2	153	FFFLRQSLTLSPRLECSGATSASPSAGITGMSHHSQPIVNFLR ACIPISK
438	1177	1	692	RQHAEERGRRNPKTGLTLERVGPESSPYLLRRHQRQGQEGEHY HSCVQLAPTRGLEES/GHGPL/SLAGGPRVGGV/AAAATEAPR MEWKVKVRSDGTRYVAKRPVRDRLLKARALKIREERSGMTTDD DAVSEMKMGRYWSKEERKQHLIRAREQRKRREFMMQSRLECLR EQQNGDSKPELNIIALSHRKTMKKRNKKILDNWITIQEMLAHG ARSADGKRVYNPLLSVTTV

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439	1178	2	616	SDRGCSAAAGRNMTAVGVQAQRPLGQRQPRRSFFESFIRTLII TCVALAVVLSSVSICDGHWLLAEDRLFGLWHFCTTTNQSVPIC FRDLGQAHVPGLAVGMGLVRSVGALAVVAAIFGLEFLMVSQLC EDKHSQCKWVMGSILLLVSFVLSSGGLLGFVILLRNQVTLIGF TLMFWCEFTASFLLFLNAISGLHINSITHPWE
440	1179	2	540	QILPNLYLGSARDSANLESLAKLGIRYILNVTPNLPNFFEKNG DFHYKQIPISDHWSQNLSRFFPEAIEFIDEALSQNCGVLVHCL AGVSRSVTVTVAYLMQKLHLSLNDAYDLVKRKKSNISPNFNFM GQLLDFERSLRLEERHSQEQGSGGQASAASNPPSFFTTPTSDG AFELAPT
441	1180	940	463	RKSLHENKLKRLQEKVEVLEAKKEELETENQVLNRQNVPFEDY TRLQKRLKDIQRRHNEFRSLILVPNMPPTASINPVSFQSSAMG SKHGTTISSSYAGGTTSKGTLSTSQKTRRTGNNTKKTTRGTWI FRRMMFLENRQIKRGEVGDSVKLDILTCGI
442	1181	1	986	GRPGAGASELFPSVTTDLSVSKQNACLTCVDFVTVHVCMGFWG IGPGALSTSCIPYPLSHGPGSVKAEMLHMYSQKDPLILCVRLA VLLAVTLTVPVVLFPIRRALQQLLFPGKAFSWPRHVAIALILL VLVNVLVICVPTIRDIFGVIGSTSAPSLIFILPSIFYLRIVPS EVEPFLSWPKIQALCFGVLGVLFMAVSLGFMFANWATGQSRMS GH*SGPAGPGPCAHAHGGVRAAP*GPSCPTCGGGWFP*TWLSE AGDSRGCRLAHFPPPQGCQAWIMALIPTPTPWEEEEEEEEEEE EEEEEEEEEARSWWSLCPAQSSLPPPG
443	1182	460	27	INELRYHLEESRDKNVLLCLEERDWDPGLAIIDNLMQSINQSK KTVFVLTKKYAKSWNFKTAFYLALQRLMDENMDVIIFILLEPV LQHSQYLRLRQRICKSSILQWPDNPKAEGLFWQTLRNVVLTEN DSRYNNMYVDSIKQY
444	1183	1682	230	DDPIKTSWTPPRYVLSMSEERHERVRKKYHILVEGDGIPPPIK SFKEMKFPAAILRGLKKKGIHHPTPIQIQGIPTILSGRDMIGI AFTGSGKTLVFTLPVIMFCLEQEKRLPFSKREGPYGLIICPSR ELARQTHGILEYYCRLLQEDSSPLLRCALCIGGMSVKEQMETI RHGVHMMVATPGRLMDLLQKKMVSLDICRYLALDEADRMIDMG FEGDIRTIFSYFKGQRQTLLFSATMPKKIQNFAKSALVKPVTI NVGRAGAASLDVIQEVEYVKEEAKMVYLLECLQKTPPPVLIFA EKKADVDAIHEYLLLKGVEAVAIHGGKDQEERTKAIEAFREGK KDVLVATDVASKGLDFPAIQHVINYDMPEEIENYVHRIGRTGR SGNTGIATTFINKACDESVLMDLKALLLEAKQKVPPVLQVLHC GDESMLDIGGERGCAFCGGLGHRITDCPKLEAMQTKQVSNIGR KDYLAHSSMDF
445	1184	1	375	IETTQPSEDTNANSQDNSMQPETSSQQQLLSPTLSDRGGSRQD AADAGKPQRKFGQWRLPSAPKPISHSVSSVNLRFGGRTTMKSV VCKMNPMTDAASCGSEVKKWWTRQLTVESDESGDDLLDI
446	1185	2	223	NDRFSACYFTLKLKEAAVRQREALKKLTKNIATDSYISVNLRD VYARSIMEMLRLKGRERASTRSSGGDDFWF

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447	1186	2	1031	FTVFILGITIRPLVEFLDVKRSNKKQQAVSEEIYCRLFDHVKT GIEDVCGHWGHNFWRDKFKKFDDKYLRKLLIRENQPKSSIVSL YKKLEIKHAIEMAETGMISTVPTFASLNDCREEKIRKVTSSET DEIRELLSRNLYQIRQRTLSYNRHSLTADTSERQAKEILIRRR HSLRESIRKDSSLNREHRASTSTSRYLSLPKNTKLPEKLQKRR TISIADGNSSDSDADAGTTVLNLQPRARRFLPEQFSKKSPQSY KMEWKNEVDVDSGRDMPSTPPTPHSREKGTQTSGLLQQPLLSK DQSGSEREDSLTEGIPPKPPPRLVWRASEPGSRKARFGSEKP
448	1187	3	444	HEEASGLSVWMGKQMEPLHAVPPAAITLILSLLVAVFTECTSN VATTTLFLPIFASMSRSIGLNPLYIMLPCTLSASFAFMLPVAT PPNAIVFTYGHLKVADMVKTGVIMNIIGVFCVFLAVNTWGRAI FDLDHFPDWANVTHIET
449	1188	3	125	HELENNWLQHEKAPTEEGKKELLALSNANPSLLERHCAYL
450	1189	1	188	GNIIYMYMQPGARSSQDQGKFLTLFYNIVTPLLNPLIYTLRNR EVKGALGRLLLGKRELGKE
451	1190	10	1879	PLEQRSNCRVDPRVRTHTMASDTSSLVQSHTYKKREPADVPYQ TGQLHPAIRVADLLQHITQMKCAEGYGFKEEYESFFEGQSAPW DSAKKDENRMKNRYGNIIAYDHSRVRLQTIEGDTNSDYINGNY IDGYHRPNHYIATQGPMQETIYDFWRMVWHENTASIIMVTNLV EVGRVKCCKYWPDDTEIYKDIKVTLIETELLAEYVIRTFAVEK RGVHEIREIRQFHFTGWPDHGVPYHATGLLGFVRQVKSKSPPS AGPLVVHCSAGAGRTGCFIVIDIMLDMAEREGVVDIYNCVREL RSRRVNMVQTEEQYVFIHDAILEACLCGDTSVPASQVRSLYYD MNKLDPQTNSSQIKEEFRTLNMVTPTLRVEDCSIALLPRNHEK NRCMDILPPDRCLPFLITIDGESSNYINAALMDSYKQPSAFIV TQHPLPNTVKDFWRLVLDYHCTSVVMLNDVDPAQLCPQYWPEN GVHRHGPIQVEFVSADLEEDIISRIFRIYNAARPQDGYRMVQQ FQFLGWPMYRDTPVSKRSFLKLIRQVDKWQEEYNGGEGRTVVH CLNGGGRSGTFCAISIVCEMLRHQRTVDVFHAVKTLRNNKPNM VDLLDQYKFCYEVALEYLNSG
452	1191	603	342	PLTYNKKYTYPWWGDALGWLLALSSMVCIPAWSLYRLGTLKGP FRERIRQLMCPAEDLPQRNPAGPSAPATPRTSLLRLTELESHC
453	1192	120	449	TLSESGALFSLGPPPLSLKSSSAPRPYSTLRDCLEHFAELFDL GFPNPLAERIIFETHQIHFANCSLGQPTFSDPPEDVLLAMIIA PICLIPFLITLVVWRSKDSEAQA
454	1193	1838	1066	CEEREQEKDDVDVALLPTIVEKVILPKLTVIAENMWDPFSTTQ TSRMVGITLKLINGYPSVVNAENKNTQVYLKALLLRMRRTLDD DVFMPLYPKNVLENKNSGPYLFFQRQFWSSVKLLGNFLQWYGI FSNKTLQELSIDGLLNRYILMAFQNSEYGDDSIKKAQNVINCF PKQWFMNLKGERTISQLENFCRYLVHLADTIYRNSIGCSDVEK RNARENIKQIVKLLASVRALDHAMSVASDHNVKEFKSLIEGK

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455	1194	112	1361	TPFCFLCSLVFRSRVWAEPCLIDAAKEEYNGVIEEFLATGEKL FGPYVWGRYDLLFMPPSFPFGGMENPCLTFVTPCLLAGDRSLA DVIIHEISHSWFGNLVTNANWGEFWLNEGFTMYAQRRISTILF GAAYTCLEAATGRALLRQHMDITGEENPLNKLRVKIEPGVDPD DTYNETPYEKGFCFVSYLAHLVGDQDQFDSFLKAYVHEFKFRS ILADDFLDFYLEYFPELKKKRVDIIPGFEFDRWLNTPGWPPYL PDLSPGDSLMKPAEELAQLWAAEELDMKAIEAVAISPWKTYQL VYFLDKILQKSPLPPGNVKKLGDTYPSISNARNAELRLRWGQI VLKNDHQEDFWKVKEFLHNQGKQKYTLPLYHAMMGGSEVAQTL AKETFASTASQLHSNVVNYVQQIVAPKGS
456	1195	1	889	CASGSSGWRPVLWAGAFTMASAELDYTIEIPDQPCWSQKNSPS PGGKEAETRQPVVILLGWGGCKDKNLAKYSAIYHKRGCIVIRY TAPWHMVFFSESLGIPSLRVLAQKLLELLFDYEIEKEPLLFHV FSNGGVMLYRYVLELLQTRRFCRLRVVGTIFDSAPGDSNLVGA LRALAAILERRAAMLRLLLLVAFALVVVLFHVLLAPITALFHT HFYDRLQDAGSRWPELYLYSRADEVVLARDIERMVEARLARRV LARSVDFVSSAHVSHLRDYPTYYTSLCVDFMR\NWVRC
457	1196	2	295	PRVRDRLPSTGVRDRKGDKPWKESGGSVEAPRMGFTHPPGHLS GCQSSLASGETGTGSADPPGGPRPGLTRRAPVKDTPGRAPAAD AAPAGPSSCLG
458	1197	1299	682	QGRTSCIGLYTYQRRICKYRDQYNWFFLARPTTFAIIENLKYF LLKKDPSQPFYLGHTIKSGDLEYVGMEGGIVLSVESMKRLNSL LNIPEKCPEQGGMIWKISEDKQLAVCLKYAGVFAENAEDADGK DVFNTKSVGLSIKEAMTYHPNQVVEGCCSDMAVTFNGLTPNQM HVMMYGVYRLRAFG\HIFNDALVFLPPNGSDND
459	1198	779	61	HEGKPTRGRGRGGSLSTRGRGSEVPDSAHLAPTPLFSESGCCG LRSRFLTDCKMEEGGNLGGLIKMVHLLVLSGAWGMQMWVTFVS GFLLFRSLPRHTFGLVQSKLFPFYFHISMGCAFINLCILASQH AWAQLTFWEASQLYLLFLSLTLATVNARWLEPRTTAAMWALQT VEKERGLGGEVPGSHQGPDPYRQLREKDPKYSALRQNFFRYHG LSSLCNLGCVLSNGLCLA\ALPWK
460	1199	517	815	KQLDKQLRADPSGSLPPLPPSPPPPLEAGGRPPEVP/PRGPSA VPSFPSVSGDWGGPVEAG/EGGQQGRGRARARPCSLPPLLPPS PVCRLSGSRAPLGCDG
461	1200	1	583	RNQLSSQKSVPWVPILKSLPLWAIVVAHFSYNWTFYTLLTLLP TYMKEILRFNVQENGFLSSLPYLGSWLCMILSGQAADNLRAKW NFSTLCVRRIFSLIGMIGPAVFLVAAGFIGCDYSLAVAFLTIS TTLGGFCSSGFSINHLDIAPSYAGILLGITNTFATIPGMVGPV IAKSLTPDMGISLHRPGWSAVA
462	1201	25	383	GPSGTTHASAHSGHPGSPRGSLSRHPSSQLAGPGVEGGEGTQK PRDYIILAILSCFCPMWPVNIVAFAYAVMSRNSLQQGDVDGAQ RLGRVAKLLSIVALVGGVLIIIASCVINLGVYK
463	1202	573	372	SLFLSFPPLSFKMTLNDAMRNKARLSITGSTGENGRVMTPEFP KAVHAVPYVSPGMGMNVSVTDLS

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464	1203	2018	491	DDVPPPAPDLYDVPPGLRRPGPGTLYDVPRERVLPPEVADGGV VDSGVYAVPPPAEREAPAEGKRLSASSTGSTRSSQSASSLEVA GPGREPLELEVAVEALARLQQGVSATVAHLLDLAGSAGATGSW RSPSEPQEPLVQDLQAAVAAVQSAVHELLEFARSAVGNAAHTS DRALHAKLSRQLQKMEDVHQTLVAHGQALDAGRGGSGATLEDL DRLVACSRAVPEDAKQLASFLHGNASLLFRRTKATAPGPEGGG TLHPNPTDKTSSIQSRPLPSPPKFTSQDSPDGQYENSEGGWME DYDYVHLQGKEEFEKTQKELLEKGSITRQGKSQLELQQLKQFE RLEQEVSRPIDHDLANWTPAQPLAPGRTGGLGPSDRQLLLFYL EQCEANLTTLTNAVDAFFTAVATNQPPKIFVAHSKFVILSAHK LVFIGDTLSRQAKAADVRSQVTHYSNLLCDLLRGIVATTKAAA LQYPSPSAAQDMVERVKELGHSTQQFRRVLGQLAAA
465	1204	299	189	EMEEPQKSYVNTMDLERDEPLKSTGPQISVSEFSCHCCYDILV NPTTLNCGHSFCRHCLALWWASSKKTECPECREKWEGFPKVSI LLRDAIEKLFPDAIRLRFEDIQQNNDIVQSLAAFQKYGNDQIP LAPNTGRANQQMGGGFFSGVLTALTGVAVVLLVYHWSSRESEH DLLVHKAVAKWTAEEVVLWLEQLGPWASLYRERFLSERVNGRL LLTLTEEEFSKTPYTIENSSHRRAILMELERVKALGVKPPQNL WEYKAVNPGRSLFLLYALKSSPRLSLLYLYLFDYTDTFLPFIH TICPLQEDSSGEDIVTKLLDLKEPTWKQWREFLVKYSFLPYQL IAEFAWDWLEVHYWTSRFLIINAMLLSVLELFSFWRIWSRSEL K*VGFRFLRLGVAALGSVEVAGLRGVVKGERPLLYGHGAGARF PHSVLLLPVAKPLPLPLLPRGLC
466	1205	2	242	EKARMIYEDYISILSPKEVSLDSRVREVINRNLLDPNPHMYED AQLQIYTLMHRDSFPRFLNSQIYKSFVESTAGSSSES
467	1206	2	619	LYYSQDEESKIMISDFGLSKMEGKGDVMSTACGTPGYVAPEVL AQKPYSKAVDCWSIGVIAYILLCGYPPFYDENDSKLFEQILKA EYEFDSPYWDDISDSAKDFIRNLMEKDPNKRYTCEQAARHPWI AGDTALNKNIHESVSAQIRKNFAKSKWRQAFNATAVVRHMRKL HLGSSLDSSNASVSSSLSLASQKDCASGTFHAL
468	1207	1	352	RTRGGAVSFEDFIKGLSILLRGTVQEKLNWAFNLYDINKDGYI TKEEMLDIMKAIYDMMGKCTYPVLKEDAPRQHVETFFQKMDKN KDGVVTIDEFIESCQKDENIMRSMQLFENVI
469	1208	3	1015	PRSPEHHTPAWHEGRSLGPIMASMADRNMKLFSGRVVPAQGEE TFENWLTQVNGVLPDWNMSEEEKLKRLMKTLRGPAREVMRVLQ ATNPNLSVADFLRAMKLVFGESESSSVTAHGKFFNTLQAQGEKA SLYVIRLEVQLQNAIQAGIIAEKDANRTRLQQLLLGGELSRDL RLRLKDFLRMYANEQERLPNFLELIKMVREEEDWDDAFIKRKR PKRSESMVERAVSPVAFQGSPPIVIGSADCNVIEIDDTLDDSD EDVILVESQDPPLPSWGAPPLRDRARPQDEVLVIDSPHNSRAQ FPSTSGGSGYKNNGPGEMRRARKRKHTIRCSYCGEE
470	1209	1543	1351	SVACTVPLRSMSDPDQDFDKEPDSDSTKHSTPSNSSNPSGPPS PNSPHRSQLPLEGLEQPACDT

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471	1210	3	952	YSAVEFAERGSGGSSGDELREDDEPVKKRGRKGRGRGPPSSSD SEPEAELEREAKKSAKKPQSSSTEPARKPGQKEKRVRPEEKQQ AKPVKVERTRKRSEGFSMDRKVEKKKEPSVEEKLQKLHSEIKF ALKVDSPDVKRCLNALEELGTLQVTSQILQKNTDVVATLKKIR RYKANKDVMEKAAEVYTRLKSRVLGPKIEAVQKVNKAGMEKEK AEEKLAGEELAGEEAPQEKAEDKPSTDLSAPVNGEATSQKGES AEDKEHEEGRDSEEGPRCGSSEDLHDSVREGPDLDRPGSDRQE RERARGDSEALDEES
472	1211	5204	2901	LAELSSLSVLRLSHNSISHIAEGAFKGLRSLRVLDLDHNEISG TIEDTSGAFSGLDSLSKLTLFGNKIKSVAKRAFSGLEGLEHLN LGGNAIRSVQFDAFVKMKNLKELHISSDSFLCDCQLKWLPPWL IGRMLQAFVTATCAHPESLKGQSIFSVPPESFVCDDFLKPQII TQPETTMAMVGKDIRFTCSAASSSSSPMTFAWKKDNEVLTNAD MENFVHVHAQDGEVMEYTTILHLRQVTFGHEGRYQCVITNHFG STYSHKARLTVNVLPSFTKTPHDITIRTTTMARLECAATGHPN PQIAWQKDGGTDFPAARERRMHVMPDDDVFFITDVKIDDAGVY SCTAQNSAGSISANATLTVLETPSLVVPLEDRVVSVGETVALQ CKATGNPPPRITWFKGDRPLSLTERHHLTPDNQLLVVQNVVAE DAGRYTCEMSNTLGTERAHSQLSVLPAAGCRKDGTTVGIFTIA VVSSIVLTSLVWVCIIYQTRKKSEEYSVTNTDETVVPPDVPSY LSSQGTLSDRQETVVRTEGGPQANGHIESNGVCPRDASHFPEP DTHSVACRQPKLCAGSAYHKKPWKAMEKAEGTPGPHKMEHGGR VVCSDCNTEVDCYSRGQAFHPQPVSRDSAQPSAPNGPEPGGSD QEHSPHHQCSRTAAGSCPECQGSLYPSNHDRMLTAVKKKPMAS LDGKGDSSWTLARLYHPDSTELQPASSLTSGSPERAEAQYLLV SNGHLPKACDASPESTPLTGQLPGKQRVPLLLAPKS

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473	1212	2	2466	AAAGAARRVSVRCGRSGPGPGRGAAGLSPADIALASEQGASCS VRAPERKLRMKLLWQAKMSSIQDWGEEVEEGAVYHVTLKRVQI QQAANKGARWLGVEGDQLPPGHTVSQYETCKIRTIKAGTLEKL VENLLTAFGDNDFTYISIFLSTYRGFASTKEVLELLLDRYGNL TSPNCEEDGSQSSSESKMVIRNAIASILRAWLDQCAEDFREPP HFPCLQKLLDYLTRMMPGSDPERRAQNLLEQFQKQEVETDNGL PNTISFSLEEEEELEGGESAEFTCFSEDLVAEQLTYMDAQLFK KVVPHHCLGCIWSRRDKKENKHLAPTIRATISQFNTLTKCVVS TILGGKELKTQQRAKIIEKWINIAHECRLLKNFSSLRAIVSAL QSNSIYRLKKTWAAVPRDRMLMFEELSDIFSDHNNHLTSRELL MKEGTSKFANLDSSVKENQKRTQRRLQLQKDMGVMQGTVPYLG TFLTDLTMLDTALQDYIEGGLINFEKRRREFEVIAQIKLLQSA CNSYCMTPDQKFIQWFQRQQLLTEEESYALSCEIEAAADASTT SPKPWKSMVKRLNLLFLGADMITSPTPTKEQPKSTASGSSGES MDSVSVSSCESNHSEAEEGYITPMDTPDEPQKKLSESSSYCSS IHSMDTNFLQGMSSLINPLSSPPSCNNNPKIHKRSVSVTSITS TVLPPVYNQQNEDTCIIRISVEDNNGNMYKSIMLTSQDKTPAV IQRAMLKHNLDSDPAEEYELVQVISEDKELVIPDSANVFYAMN SQVNFDFILRKKNSMEEQVKLRSRTSLTLPRTAKRGCWSNRHS KITL
474	1213	1	867	AREKMDSCIEAFGTTKQKRALNTRRMNRVGNESLNRAVAKAAE TIIDTKGVTALVSDAIHNDLQDDSLYLPPCYDDAAKPEDVYKF EDLLSPAEYEALQSPSEAFRNVTSEEILKMIEENSHCTFVIEA LKSLPSDVESRDRQARCIWFLDTLIKFRAHRVVKRKSALGPGV PHIINTKLLKHFTCLTYNNGRLRNLISDSMKAKITAYVIILAL HIHDFQIDLTVLQRDLKLSEKRMMEIAKAMRLKISKRRVSVAA GSEEDHKLGTLSLPLPPAQTSDRLAKRRKIT

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475	1214	2	2621	LSLFGSRALGRSGARAMAKAKKVGARRKASGAPAGARGGPAKA NSNPFEVKVNRQKFQILGRKTRHDVGLPGVSRARALRKRTQTL LKEYKERDKSNVFRDKRFGEYNSNMSPEEKMMKRFALEQQRHH EKKSIYNLNEDEELTHYGQSLADIEKHNDIVDSDSDAEDRGTL SGELTAAHFGGGGGLLHKKTQQEGEEREKPKSRKELIEELIAK SKQEKRERQAQREDALELTEKLDQDWKEIQTLLSHKTPKSENR DKKEKPKPDAYDMMVRELGFEMKAQPSNRMKTEAELAKEEQEH LRKLEAERLRRMLGKDEDENVKKPKHMSADDLNDGFVLDKDDR RLLSYKDGKMNVEEDVQEEQSKEASDPESNEEEGDSSGGEDTE ESDSPDSHLDLESNVESEEENEKPAKEQRQTPGKGLISGKERA GKATRDELPYTFAAPESYEELRSLLLGRSMEEQLLVVERIQKC NHPSLAEGNKAKLEKLFGFLLEYVGDLATDDPPDLTVIDKLVV HLYHLCQMFPESASDAIKFVLRDAMHEMEEMIETKGRAALPGL DVLIYLKITGLLFPTSDFWHPVVTPALVCLSQLLTKCPILSLQ DVVKGLFVCCLFLEYVALSQRFIPELINFLLGILYIATPNKAS QGSTLVHPFRALGKNSELLVVSAREDVATWQQSSLSLRWASRL RAPTSTEANHIRLSCLAVGLALLKRCVLMYGSLPSFHAIMGPL RALLTDHLADCSHPQELQELCQSTLTEMESQKQLCRPLTCEKS KPVPLKLFTPRLVKVLEFGRKQGSSKEEQERKRLIHKHKREFK GAVREIRKDNQFLARMQLSEIMERDAERKRKVKQLFNSLATQE GEWKALKRKKFKK
476	1215	3	961	LTKQEDCCGSIGTAWGQSKCHKCPQLQYTGVQKPGPVRGEVGA DCPQGYKRLNSTHCQDINECAMPGVCRHGDCLNNPGSYRCVCP PGHSLGPSRTQCIADKPEEKSLCFRLVSPEHQCQHPLTTRLTR QLCCCSVGKAWGARCQRCPTDGTAAFKEICPAGKGYHILTSHQ TLTIQGESDFSLFLHPDGPPKPQQLPESPSQAPPPEDTEEERG VTTDSPVSEERSVQQSHPTATTTPARPYPELISRPSPPTMRWF LPDLPPSRSAVEIAPTQVTETDECRLNQNICGHGECVPGPPDY SCHCNPGYRSHPQHRYCV

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477	1216	3652	1207	MAGGHCGSFPAAAAGSGEIVQLNVGGTRFSTSRQTLMWIPDSF FSSLLSGRISTLRDETGAIFIDRDPAAFAPILNFLRTKELDLR GVSINVLRHEAEFYGITPLVRRLLLCEELERSSCGSVLFHGYL PPPGIPSRKINNTVRSADSRNGLNSTEGEARGNGTQPVLSGTG EETVRLGFPVDPRKVLIVAGHHNWIVAAYAHFAVWYRIKESSG WQQVFTSPYLDWTIERVALNAKVVGGPHGDKDKMVAVASESSI ILWSVQDGGSGSEIGVFSLGVPVDALFFIGNQLVATSHTGKVG VWNAVTQHWQVQDVVPITSYDTAGSFLLLGCNNGSIYYIDMQK FPLRMKDNDLLVTELYHDPSNDAITALSVYLTPKTSVSGNWIE IAYGTSSGAVRVIVQHPETVGSGPQLFQTFTVHRSPVTKIMLS EKHLVSVCADNNHVRTWTVTRFRGMISTQPGSTPLASFKILSL EETESHGSYSSGNDIGPFGERDDQQVFIQKVVPITNKLFVRLS STGKRICEIQAVDCTTISSFTGRECEGSSRMGSRPRRYLFTGH TNGSIQMWDLTTAMDMVNKSEDKDVGGPTEEELLKLLDQCDLS TSRCATPNISPATSVVQHSHLRESNSSLQLQHHDTTHEAATYG SMRPYRESPLLARARRTESFHSYRDFQTINLNRNVERAVPENG NLGPIQAEVKGATGECNISERKSPGVEIKSLRELDSGLEVHKI AEGFSESKKRSSEDENENKIEFRKKGGFEGGGFLGRKKVPYLA SSPSTSDGGTDSPGTASPSPTKTTPSPRHKKSDSSGQEYSL
478	1217	1	1379	RRPTRPILTDELFKRTIQLPHLKTLILNGNKLETLSLVSCFAN NTPLEHLDLSQNLLQHKNDENCSWPETVVNMNLSYNKLSDSVF RCLPKSIQILDLNNNQIQTVPKETIHLMALRELNIAFNFLTDL PGCSHFSRLSVLNIEMNFILSPSLDFVQSCQEVKTLNAGRNPF RCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLNLRGTRLKDV HLHELSCNTALLIVTIVVIMLVLGLAVAFCCLHFDLPWYLRML GQCTQTWHRVRKTTQEQLKRNVRFHAFISYSEHDSLWVKNELI PNLEKEDGSILICLYESYFDPGKSISENIVSFIEKSYKSIFVL SPNFVQNEWCHYEFYFAHHNLFHENSDHIILILLEPIPFYCIP TRYHKLKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLAT REMYELQTFTELNEESRGSTISLMRTDCL
479	1218	1	1099	PTRPPTRPPTRPLLTPSWTSTGRMWSHLNRLLFWSIFSSVTCR KAVLDCEAMKTNEFPSPCLDSKTKVVMKGQNVSMFCSHKNKSL QITYSLFRRKTHLGTQDGKGEPAIFNLSITEAHESGPYKCKAQ VTSCSKYSRDFSFTIVDPVTSPVLNIMVIQTETDRHITLHCLS VNGSLPINYTFFENHVAISPAISKYDREPAEFNLTKKNPGEEE EYRCEAKNRLPNYATYSHPVTMPSTGGDSCPFCLKLLLPGLLL LLVVIILILAFWVLPKYKTRKAMRNNVPRDRGDTAMEVGIYAN ILEKQAKEESVPEVGSRPCVSTAQDEAKHSQELQYATPVFQEV APREQEACDSYKSGYVYSELNF
480	1219	1	293	FFFFEERRTGSHSVGHPRMEYSGVSMAHCSLNLLGSSNSPSSA SQDARTTGACQHAQLIGFFFF\VETASPQVTHAG/LKHLVSRN PSAVTSQSARIKT

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481	1220	1	727	NREGARKIQNKWLRPSPRSHRTPESVSPERYSYGTSSSSKRTE GSCRRRRQSSSSANSQQGQWETGSPPTKRQRRSRGRPSGGAKR RRRGAPAAPQQQSEPARPSSEGKVTCDIRLRVRAEYCEHGPAL EQGVASRRPQALARQLDVFGQATAVLRSRDLGSVVCDIKFSEL SYLDAFWGDYLSGALLQALRGVFLTEALREAVGREAVRLLVSV DEADYEAGRRRLLLMEEEGGRRPTEAS
482	1221	1	1321	APNTAELRICRVNKNCGSVRGGDEIFLLCDKVQKDDIEVRFVL NDWEAKGIFSQADVHRQVAIVFKTPPYCKAITEPVTVKMQLRR PSDQEVSESMDFRYLPDEKDTYGNKAKKQKTTLLFQKLCQDHV ETGFRHVDQDGLELLTSGDPPTLASQSAGITVNFPERPRPGLL GSIGEGRYFKKEPNLFSHDAVVREMPTGVSSQAESYYPSPGPI SSGLSHHASMAPLPSSSWSSVAHPTPRSGNTNPLSSFSTRTLP SNSQGIPPFLRIPVGNDLNASNACIYNNADDIVGMEASSMPSA DLYGISDPNMLSNCSVNMMTTSSDSMGETDNPRLLSMNLENPS CNSVLDPRDLRQLHQMSSSSMSAGANSNTTVFVSQSDAFEGSD FSCADNSMINESGPSNSTNPNSHGFVQDSQYSGIGSMQNEQLS DSFPYEFFQV
483	1222	1	1311	RRLSLLDLQLGPLGRDPPQECSTFSPTDSGEEPGQLSPGVQFQ RRQNQRRFSMEDVSKRLSLPMDIRLPQEFLQKLQMESPDLPKP LSRMSRRASLSDIGFGKLETYVKLDKLGEGTYATVFKGRSKLT ENLVALKEIRLEHEEGAPCTAIREVSLLKNLKHANIVTLHDLI HTDRSLTLVFEYLDSDLKQYLDHCGNLMSMHNVKIFMFQLLRG LAYCHHRKILHRDLKPQNLLINERGELKLADFGLARAKSVPTK TYSNEVVTLWYRPPDVLLGSTEYSTPIDMWGVGCIHYEMATGR PLFPGSTVKEELHKINRLLGTPTEETWPGVTAFSEFRTYSFPC YLPQPLINHAPRLDTDGIHLLSSLLLYESKSRMSAEAALSHSY FRSLGERVHQLEDTASIFSLKEIQLQKDPGYRGLAFQQPGRGK NRRQSIF
484	1223	807	356	CTPHGSSSSWKIPLWPRHMSPLHSCLPVGTSTSSGPLAVPRDC FHLCCLWGQLLLISCPLACGQGCRVAGGQQHVPGQALGTLSPL VSLLTWAGPSLDWPHPGSLVTPRCPILPAVPVLVKGLGGWPPT RPSRAAPVSGPWDQLPYFPGL
485	1224	1199	370	LISPVWGNIQRSRSVPLFPSGLVLGGIWARGPLLALLASFNII SVLNAECYLKQILHPTSHFTVSETPPLSGNDTDSLSCDSGSSA TSTPCVSRLVTGHHLWASKNGRHVLGLIEDYEALLKQISQGQR LLAEMDIQTQEAPSSTSQELGTKGPHPAPLSKFVSSVSTAKLT LEEAYRRLKLLWRVSLPEDGQCPLHCEQIGEMKAEVTKLHKKL FEQEKKLQNTMKLLQLSKRQEKVIFDQLVVTHKILRKARGNLE LRPGGAHPGTCSPSRPGS

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486	1225	2469	1660	LGLFCILPIDTLCAVLERDTLSIRESRLFGAVVRWAEAECQRQ QLPVTFGNKQKVLGKALSLIRFPLMTIEEFAAGPAQSGILSDR EVVNLFLHFTVNPKPRVEYIDRPRCCLRGKECCINRFQQVESR WGYSGTSDRIRFTVNRRISIVGFGLYGSIHGPTDYQVNIQIIE YEKKQTLGQNDTGFSCDGTANTFRVMFKEPIEILPNVCYTACA TLKGPDSHYGTKGLKKVVHETPAASKTVFFFFSSPGNNNGTSI EDGQIPEIIFYT
487	1226	1193	372	SVWWNSEVKDWMQKKRRGLRNSRATAGDIAHYYRDYVVKKGLG HNFVSGAVVTAVEWGTPDPSSCGAQDSSPLFQVSGFLTRNQAQ QPFSLWARNVVLATGTFDSPARLGIPGEALPFIHHELSALEAA TRVGAVTPASDPVLIIGAGLSAADAVLYARHYNIPVIHAFRRA VDDPGLVFNQLPKMLYPEYHKVHQMMREQSILSPSPYEGYRSL PRHQLLCFKEDCQAVFQDLEGVEKVFGVSLVLVLIGSHPDLSF LPGAG\LTLQWILTSR
488	1227	756	1016	KLRPFIFSNQSLWLHSYEGAELEKTFIKGSWATFWVKVASCWA CVLLYLGLLLAPLCWPPTQKPQPLILRRRRHRIISPDNKYPPV
489	1228	1	747	QLIHLSHGYQIHWTDYYNVGTGRPEFGTRAAHKSLAGAELKTL KDFVTVLAKLFPGRPPVKKLLEMLQEWLASLPLDRIPYNAVLD LVNNKMRISGIFLTNHIKWVGCQGSRSELRGYPCSLWKLFHTL TVEASTHPDALVGTGFEDDPQAVLQTMRRYVHTFFGCKECGEH FEEMAKESMDSVKTPDQAILWLWKKHNMVNGRLAGEKPLGMGG SARAEGGPGPGTARTARLPWGLSLSFAASCHPLC
490	1229	4797	2398	HGGATFINAFVTTPMCCPSRSSMLTGKYVHNHNVYTNNENCSS PSWQAMHEPRTFAVYLNNTGYRTAFFGKYLNEYNGSYIPPGWR EWLGLIKNSRFYNYTVCRNGIKEKHGFDYAKDYFTDLITNESI NYFKMSKRMYPHRPVMMVISHAEPHGPEDSAPQFSKLYPNASQ HITPSYNYAPNMDKHWIMQYTGPMLPIHMEFTNILQRKRLQTL MSVDDSVERLYNMLVETGELENTYIIYTADHGYHIGQFGLVKG KSMPYDFDIRVPFFIRGPSVEPGSIVPQIVLNIDLAPTILDIA GLDTPPDVDGKSVLKLLDPEKPGNRFRTNKKAKIWRDTFLVER GKFLRKKEESSKNIQQSNHLPKYERVKELCQQARYQTACEQPG QKWQCIEDTSGKLRIHKCKGPSDLLTVRQSTRNLYARGFHDKD KECSCRESGYRASRSQRKSQRQFLRNQGTPKYKPRFVHTRQTR SLSVEFEGEIYDINLEEEEELQVLQPRNIAKRHDEGHKGPRDL QASSGGNRGRMLADSSNAVGPPTTVRVTHKCFILPNDSIHCER ELYQSARAWKDHKAYIDEEIEALQDKIKNLREVRGHLKRRKPE ECSCSKQSYYNKEKGVKKQEKLKSHLHPFKEAAQEVDSKLQLF KENNRRRKKERKEKRRQRKGEECSLPGLTCFTHDNNHWQTAPF WNLGSFCACTSSNNNTYWCLRTVNETHNFLFCEFATGFLEYFD MNTDPYQLTNTVHTVERGILNQLHVQLMELRSCQGYKQCNPRP KNLDVGNKDGGSYDLHRGQLWDGWEG

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491	1230	2480	385	HLLIAQELADRVGEGRACWSLGNAYVSMGRPAQALTFAKKHLQ ISQEIGDRHGELTARMNVAQLQLVLGRLTSPAASEKPDLAGYE AQGARPKRTQRLSAETWDLLRLPLEREQNGDSHHSGDWRGPSR DSLPLPVRSRKYQEGPDAERRPREGSHSPLDSADVRVHVPRTS IPRAPSSDEECFFDLLTKFQSSRMDDQRCPLDDGQAGAAEATA APTLEDRIAQPSMTASPQTEEFFDLIASSQSRRLDDQRASVGS LPGLRITHSNAGHLRGHGEPQEPGDDFFNMLIKYQSSRIDDQR CPPPDVLPRGPTMPDEDFFSLIQRVQAKRMDEQRVDLAGGPGA GGRRPARAPAAVPAWCELRPCAHRQAHPAPTPGRRSHSHSHVL PRPLPRTGTGHAAPRPPRPRATGSGQAARGGRACFHPGLAPMA LSFLPSAPAAGRTGPSACRPRPGAVRLPHPLPQALPVLPCPAK CETLLSPSPSPKVSLSRLLGPPRTGPCSVPPELVLGWPCDRHA PPLQLRPGAGLPPSLSPHSPARGQQPQKAPQTTHGRPGCSGSP EVPPAESQGPAGASTGAGPISKAEGMAGHELRHSKTPSQEKGQ GLVLGMLTGSKSSAQSGWEVAPGSVTLTQVGGWSVEAGEASLS STLQTPHMRTPLLPPAGGDDITALSMGRGLTGHQVRDPRTGRT CWSLRWAPGA
492	1231	3	398	NSAADLAIFALWGLKPVVYLLASSFLGLGLHPISGHFVAEHYM FLKGHETYSYYGPLNWITFNVGYHVEHHDFPSIPGYNLPLVRK IAPEYYDHLPQHHSWVKVLWDFVFEDSLGPYARVKRVYRLAKD GL
493	1232	1	214	QESGFSCKGPGQNVAVTRAHPDSQGRRRRPERGARGGQVFYNS EYGELSEPSEEDHCSPSARVTFFTDNSY
494	1233	3	443	VIVHARPIRTRASKYYIPEAVYGLPAYPAYAGGGGFVLSGATL HRLAGACAQVELFPIDDVFLGMCLQRLRLTPEPHPAFRTFGIP QPSAAPHLSTFDPCFYRELVVVHGLSAADIWLMWRLLHGPHGP ACAHPQPVAAGPFQWDS
495	1234	1	897	MASAACSMDPIDSFELLDLLFDRQDGILRHVELGEGWGHVKDQ VLPNPDSDDFLSSILGSGDSLPSSPLWSPEGSDSGISEDLPSD PQDTPPRSGPATSPAGCHPAQPGKGPCLSYHPGNSCSTTTPGP VIQQQHHLGASYLLRPGAGHCQELVLTEDEKKLLAKEGITLPT QLPLTKYEERVLKKIRRKIRNKQSAQESRKKKKEYIDGLETRS CCCPLPSSSSPPSALLAPTKPRALGTLRLYECSPELCTTMLPP AWLLMLCQAPRPQDPDPRLTQPEKSLQEAPGQTGASRTPRT

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496	1235	4235	940	ARGRRSRPVWAASWGGRGRPAARRRPRGLAATMGFELDRFDGD VDPDLKCALCHKVLEDPLTTPCGHVFCAGCVLPWVVQEGSCPA RCRGRLSAKELNHVLPLKRLILKLDIKCAYATRGCGRVVKLQQ LPEHLERCDFAPARCRHAGCGQVLLRRDVEAHMRDACDARPVG RCQEGCGLPLTHGEQRAGGHCCARALRAHNGALQARLGALHKA LKKEALRAGKREKSLVAQLAAAQLELQMTALRYQKKFTEYSAR LDSLSRCVAAPPGGKGEETKSLTLVLHRDSGSLGFNIIGGRPS VDNHDGSSSEGIFVSKIVDSGPAAKEGGLQIHDRIIEVNGRDL SRATHDQAVEAFKTAKEPIVVQVLRRTPRTKMFTPPSESQLVD TGTQTDITFEHIMALTKMSSPSPPVLDPYLLPEEHPSAHEYYD PNDYIGDIHQEMDREELELEEVDLYRMNSQDKLGLTVCYRTDD EDDIGIYISEIDPNSIAAKDGRIREGDRIIQINGIEVQNREEA VALLTSEENKNFSLLIARAELQLDEGWMDDDRNDFLDDLHMDM LEEQHHQAMQFTASVLQQKKHDEDGGTTDTATILSNQHEKDSG VGRTDESTRNDESSEQENNGDDATASSNPLAGQRKLTCSQDTL GSGDLPFSNKSFISPECTGAAYLGIPVDECERFRELLELKCQV KSATPYGLYYPSGPLDAGKSDPESVDKELELLNEELRSIELEC LSIVRAHKMQQLKEQYRESWMLHNSGFRNYNTSIDVRRHELSD ITELPEKSDKDSSSAYNTGESCRSTPLTLEISPDNSLRRAAEG ISCPSSEGAVGTTEAYGPASKNLLSITEDPEVGTPTYSPSLKE LDPNQPLESKERRASDGSRSPTPSQKLGSAYLPSYHHSPYKHA HIPAHAQHYQSYMQLIQQKSAVEYAQSQMSLVSMCKDLSSPTP SEPRMEWKVKIRSDGTRYITKRPVRDRLLRERALKIREERSGM TTDDDAVSEMKMGRYWSKEERKQHLVKAKEQRRRREFMMQSRL DCLKEQQAADDRKEMNILELSHKKMMKKRNKKIFDNWMTIQEL LTHGTKSPDGTRVYNSFLSVTTV
497	1236	2	157	FFFLVEMGFCHVGQGGLTLIGSSNLPASASKSAGITGVSHCAR PDFKSCVE
498	1237	1	211	LAGRKVLLFVSGYVVGWGPITWLLMSEVLPLRARGVASGLCVL ASWLTAFVLTKSFLPGGVSVQPQAPGP
499	1238	2	345	FWAPGPPGVGAAVGDASTRSLRESCPSPSPGRLRRTTAPWSSQ ARAAAPAPSSSCRGPDGASSPRDLPWRPWKILRRTPLSGDVEL SQVHPDQRILRRFILSRTCGNTIPGMAE
500	1239	1	523	MRRFLSKVYSFPMRKLILFLVFPVVRQTPTQHFKNQFPALHWE HELGLAFTKNRMNYTNKFLLIPESGDYFIYSQVTFRGMTSECS EIRQAGRPNKPDSITVVITKVTDSYPEPTQLLMGTKSVCEVGS NWFQPIYLGAMFSLQEGDKLMVNVSDISLVDYTKEDKTFFGAF LL

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501	1240	2	1277	FVWDEVAQRSGCEERWLVIDRKVYNISEFTRRHPGGSRVISHY AGQDATDPFVAFHINKGLVKKYMNSLLIGELSPEQPSFEPTKN KELTDEFRELRATVERMGLMKANHVFFLLYLLHILLLDGAAWL TLWVFGTSFLPFLLCAVLLSAVQAQAGWLQHDFGHLSVFSTSK WNHLLHHFVIGHLKGAPASWWNHMHFQHHAKPNCFRKDPDINM HPFFFALGKILSVELGKQKKKYMPYNHQHKYFFLIGPPALLPL YFQWYIFYFVIQRKKWVDLAWMITFYVRFFLTYVPLLGLKAFL GLFFIVRFLESNWFVWVTQMNHIPMHIDHDRNMDWVSTQLQAT CNVHKSAFNDWFSGHLNFQIEHHLFPTMPRHNYHKVAPLVQSL CAKHGIEYQSKPLLSAFADIIHSLKESGQLWLDAYLHQ
502	1241	999	540	QCGGIPYNTTQFLMNDRDPEEPNLDVPHGISHPGSSGESEAGD SDGRGRAHGEFQRKDFSETYERFHTESLQGRSKQELVRDYLEL EKRLSQAEEETRRLQQLQACTGQQSCRQVEELAAEVQRLRTEN QRLRQENQMWNREGCRCDEEPGT
503	1242	1448	875	SPERSSLSVGREKAMEVPPPAPRSFLCRALCLFPRVFAAEAVT ADSEVLEERQKRLPYVPEPYYPESGWDRLRELFGKD\VTGSLF RINVGLRGLVAGGIIGALLGTPVGGLLMAFQKYSGETVQERKQ KDRKALHELKLEEWKGRLQVTEHLPEKIESSLQEDEPENDAKK IEALLNLPRNPSVIDKQDKD
504	1243	149	1293	RSLGLAVTEMVPWVRTMGQKLKQRLRLDVGREICRQYPLFCFL LLCLSAASLLLNRYIHILMIFWSFVAGVVTFYCSLGPDSLLPN IFFTIKYKPKQLGLQELFPQGHSCAVCGKVKCKRHRPSLLLEN YQPWLDLKISSKVDASLSEVLELVLENFVYPWYRDVTDDESFV DELRITLRFFASVLIRRIHKVDIPSIITKKLLKAAMKHIEVIV KARQKVKNTEFLQQAALEEYGPELHVALRSRRDELHYLRKLTE LLFPYILPPKATDCRSLTLLIREILSGSVFLPSLDFLADPDTV NHLLIIFIDDSPPEKATEPASPLVPFLQKFAEPRNKKPSVLKL ELKQIREQQDLLFRFMNFLKQEGAVHVLHVLFDCGGI
505	1244	2	1116	QSLAEVLQQLGASSELQAVLSYIFPTYGVTPNHSAFSMHALLV NHYMKGGFYPRGVTSEIAFHTIPVIQRAGGAVLTKATVQSVLL DSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNA RCLPGVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYYVY YDTDMDQAMERYVSMPREEAAEHIPLLFFAFPSAKDPTWEDRF PGRSTMIMLIPTAYEWFEEWQAELKGK\RGSDYETFKNSFVEA SMSVVLKLFPQLEGKVESVTAGSPLTNQFYL\AAPRGACYGAD HDLGRLHPCVMASLRAQSPIPNLYLTGQDIFTCGLVGALQGAL LCSSTILKRNLYSDLKNLDSRIRAQKKKN
506	1245	1759	873	RPQETRVLQVSCGRAHSLVLTDREGVFSMGNNSYGQCGRKVVE NEIYSESHRVHRMQDFDGQVVQVACGQDHSLFLTDKGEVYSCG WGADGQTGLGHYNITSSPTKLGGDLAGVNVIQVATYGDCCLAV SADGGLFGWGNSEYLQLASVTDSTQVNVPRCLHFSGVGKVRQA ACGGTGCAVLNGEGHVFVWGYGILGKGPNLVESAVPEMIPPTL FGLTEFNPEIQVSRIRCGLSHFAALTNKGELFVWGKNIRGCLG IGRLEDQYFPWRVTMPGEPVDVACGVDHMVTLAKSFI

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507	1246	520	2	LPFREWLMIVVSLSAAAVAAAFMAKCRMVLSSRYFCSHFVMSA SRARIRSSFSRTSSRRAGALYSGMLAGWPFPCFCWVLSASSSL SSQVRSLRSICSRFSHADCSWVRACCSFSTFSTYACFSRNSSS SLMTLAWALLKAWSRISMCLRWSSLAVRTAANSISNFSFSFKN
508	1247	1	1083	MQAVRATASQSLSCARAPREPTQHALRAHWFPPAAAVQPSPHS GVAAAAGTWSSAFRGEHPLVSSGLLLGVREQSFRLLRSKAGTH MYLEHTSHCPHHDDDTAMDTPLPRPRPLLAVERTGQRPLWAPS LELPKPDMQPLPAGAFLEEVAEGTPAQTESEPKVLDPEEDLLC IAKTFSYLRESGWYWGSITASEARQHLQKMPEGTFLVRDSTHP SYLFTLSVKTTRGPTNVRIEYADSSFRLDSNCLSRPRILAFPD VVSLVQHYVASCTADTRSDSPDPAPTPALPMPKEDAPSDPALP APPPATAVHLKLVQPFVRRSSARSLQHLCRLVINRLVADVDCL PLPRRMADYLRQYPFQL
509	1248	2	841	FVDIFQRWKECRGKSPAQAELSYLNKAKWLEMYGVDMHVVRGR DGCEYSLGLTPTGILIFEGANKIGLFFWPKITKMDFKKSKLTL VVVEDDDQGREQEHTFVFRLDSARTCKHLWKCAVEHHAFFRLR TPGNSKSNRSDFIRLGSRFRFSGRTEYQATHGSRLRRTSTFER KPSKRYPSRRHSTFKASNPVIAAQLCSKTNPEVHNYQPQYHPN IHPSQPRWHPHSPNVRPSFQDDRSHWKASASGDDSHFDYVHDQ NQKNLGGMQSMMYRDKLMTAL
510	1249	2	763	GGIRLIQKLTWRSRQQDRENCAMKGKHKDECHNFIKVFVPRND EMVFVCGTNAFNPMCRYYRVSIFYVICFF*STFLPSLICC*S* NLSAFQ*FVLSLVQ*KNKDRILQMEF*YK*NSIAFKRAR*IDM TLAIYFSFV\LSTL*YDGEEISGLARCPFDARQTNGALFADGK LYSATVADFLASDAVIYRSMGDGSALRTIKYDSKWIKE/PHFL YAIK/Y/GNYVYFSFREIVAT**LG/KAVDS/RVARYEKQLVG PTV
511	1250	1555	629	ARALARERESESARADDVTLGVSAILAVDRGGNLGSA\DGWAY IDVEVRRPWAFVGPGCSRSSGNGSTAYGLVGSPRWLSPFHTGG AVSLPRRPRGPGPVLGVARPCLRCVLRPE\HYEPGSHYSGFAG RDASRAFVTGDCSEAGLVDDVSDLSAAEMLTLHNWLSFYEKNY VCVGRVTGRFYGEDGLPTPALTQVEAAITRGLEANKLQLQEKQ TFPPCNAEWSSARGSRLWCSQKSGGVSRDWIGVPRKLYKPGAK EPRCVCVRTTGPPSGQMPDNPPHRNRGDLDHPNLAEYTGCPPL AITCSFPL
512	1251	1100	798	YFIICRDGVLLFCPGWSQTPGAQAILLHWATQNAGMTDMSHSA QPIYLFIYLIRTRSHYVAQAGQLLDSNDSPNVASQNVGITGMS HHAWLKIVLYFCII

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513	1252	3	1395	PAARPPSLVRLSPSPPKPRARARAPQSVEPAAPLVARGSSPPA RPAPAMVRPRRAPYRSGAGGPLGGRGRPPRPLVVRAVRSRSWP ASPRGPQPPR\IRARSAPPMEGARVFGALGPIGPSSPGLTLGG LAVSEHRLSNKLLAWSGVLEWQEKRRPYSDSTAKLKRTLPCQA YVNQGENLETDQWPQKLIMQLIPQQLLTTLGPLFRNSQLAQFH FTNRDCDSLKGLCRIMGNGFAGCMLFPHISPCEVRVLMLLYSS KKKIFMGLIPYDQSGFVSAIRQVITTRKQAVGPGGVNSGPVQI VNNKFLAWSGVMEWQEPRPEPNSRSKRWLPSHVYVNQGEILRT EQWPRKLYMQLIPQQLLTTLVPLFRNSRLVQFHFTKDLETLKS LCRIMDNGFAGCVHFSYKASCEIRVLMLLYSSEKKIFIGLIPH DQGNFVNGIRRVIANQQQVLQRNLEQEQQQRGMGG
514	1253	320	964	GRPALGREAPPQAGLSSTPPPCSETCTMGPHSILRTVHCRPTK TPPEPSAEPHPLSLLTSSNTSLAGTSLGRDLTPGGGKPPSGQT PRNPESPRHRLGSPRGRRWLASPTPTGSGRSGPASRGQRRLSC AAQDPTSEGASVGAMEAGLGPPTAAPRGVVSEAAESLGGTLSW GAWGRPPAGPSGLAGRRSRREALRPDRKEASVMMAAVSAIQP
515	1254	704	107	PGVPTHGWPRSRVLTRVRGSRGSGKMAAAVVLAAGLRAARRAV AATGVRGGQVRGAAGVTDGNEVAKAQQATPGGAAPTIFSRILD KSLPADILYEDQQCLVFRDVAPQAPVHFLVIPKKPIPRISQAE EEDQQ/LTYVPPLSL*LLGHLLLVAKQTAKAEGLGDGYRLVIN DGKLGAQSVYHLHIHVLGGRQLQWPPG
516	1255	2299	924	VPNYLPSVSSAIGGEVPQRYVWRFCIGLHSAPRFLVAFAYWNH YLSCTSPCSCYRPLCRLNFGLNVVENLALLVLTYVSSSEDF/T WVPG*GRSGEVFPEGTGLPLPHSDLPTSWCGHSLQCGSQSSFP PAIHENAFIVFIASSLGHMLLTCILWRLTKKHTVSQE\DGLSL AGAPRQPRRKSRTSVLRIRVMVRWELSSNGNPGRGVLGLGLGL GNKLRVVGQNLGL*HCVWVVWETGE*KRWRLQMGIE*GVASRR Q*VRNSVRGLVCHNSSAPPMYMGFFSPTVFGGGVGG*LHVTFI LHPPEVEAAGIPLLLGPSLPQRQGREHIVVILAAPACAPFHDR *WEPREIRPSP*ELGLRGEPTLSYPASCRVIRQPIP*DRKSYS WKQRLFIINFISFFSALAVYFRHNMYCEAGVYTIFAILEYTVV LTNMAFHMTAWWDFGNKELLITSQPEEKRF
517	1256	3	254	IDLLEIRNGPRSHESFQEMDLNDDWKLSKDEVKAYLKKEFEKH GAVVNESHHDALVEDIFDKEDEDKDGFISAREFTYKHDEL
518	1257	2	611	PRVRGRVGKEGAAAKPRSLLRRFQLLSWSVCGGNKDPWVQELM SCLDLKECGHAYSGIVAHQKHLLPTSPPISQASEGASSDIHTP AQMLLSTLQSTQRPTLPVGSLSSDKELTRPNETTIHTAGHSLA AGPEAGENQKQPEKNAGPTARTSATVPVLCLLAIIFILTAALS YVLCKRRRGQSPQSSPDLPVHYIPVAPDSNT
519	1258	1002	418	LIISNFLKAKQKPGSTPNLQQKKSQARLAPDIVSASQYRKFDE FQTGILIYELLHQPNPFEVRAQLRERDYRQEDLPPLPALSLYS PGLQQLAHLLLEADPIKRIRIGEAKRVLQCLLWGPRRELVQQP GTSEEALCGTLHNWIDMKRALMMMKFAEKAVDRRRGVELEDWL CCQYLASAEPGALLQSLKLLQLL

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520	1259	2	2019	KRGLIVVMAHEMIGTQIVTERGVALLESGTEKVLLIDSRPFVE YNTSHILEAININCSKLMKRRLQQDKVLITELIQHSAKHKVDI DCSQKVVVYDQSSQDVASLSSDCFLTVLLGKLEKSFNSVHLLA GGFAEFSRCFPGLCEGKSTLVPTCISQPCLPVANIGPTRILPN LYLGCQRDVLNKELMQQNGIGYVLNASNTCPKPDFIPESHFLR VPVNDSFCEKILPWLDKSVDFIEKAKASNGCVLVHCLAGISRS ATIAIAYIMKRMDMSLDEAYRFVKEKRPTISPNFNFLGQLLDY EKKIKNQTGASGPKSKLKLLHLEKPNEPVPAVSEGGQKSETPL SPPCADSATSEAAGQRPVHPASVPSVPSVQPSLLEDSPLVQAL SGLHLSADRLEDSNKLKRSFSLDIKSVSYSASMAASLHGFSSS EDALEYYKPSTTLDGTNKLCQFSPVQEL/CGADSRNQS**GGS Q/PSPRSCRPPGLQTARASDCIRSEPAAVAPPRGPFYLHCIEV GAWRTITTPASFSAFPP\PAAPHEVCWPGP*GLA\PDILAPQT STPSLTSSWYFATESSHFYSASAIYGGSASYSAYSCSQLPTCG DQVYSVRRRQKPSDRADSRRSWHEESPFEKQFKRRSCQMEFGE SIMSENRSREELGKVGSQSSFSGSMEIIEVS
521	1260	20	803	ASSSKRVSRQKMLQLWKLVLLCGVLTGTSESLLDNLGNDLSNV VDKLEPVLHEGLETVDNTLKGILEKLKVDLGVLQKSSAWQLAK QKAQEAEKLLNNVISKLLPTNTDIFGLKISNSLILDVKAEPID DGKGLNLSFPVTANVTEAGPIIDQIIN\LRASLDLLTAVTIET DPQTHHPVAGLGECARDPTSISLCLLDKHSQIINKFVNSVINT LKSTVSSLLQKEICPLIRIFIHSLDVNVIQQVVDNPQHKTQLQ TLI
522	1261	1246	411	CSLRRPRSAAEPDADHVPLLGLLRLQLRAARQPGAMRPQGPAA SPQRLRGLLLLLLLQLPAPSSASEIPKGKQKAQLRQREVVDLY NGMCLQGPAGVPGRDGSPGANGIPGTPGIPGRDGFKGEKGECL RESFEESWTPNYKQCSWSSLNYGIDLGKIAECTFTKMRSNSAL RVLFSGSLRLKCRNACCQRWYFTFNGAECSGPLPIEAIIYLDQ GSPEMNSTINIHRTSSVEGLCEGIGAGLVDVAIWVGTCSDYPK GDASTGWNSVSRIIIEELPK
523	1262	2009	921	MHSAMLGTRVNLSVSDFWRVMMRVCWLVRQDSRHQRIRLPHLE AVVIGRGPETKITDKKCSRQQVQLKAECNKGYVKVKQVGVNPT SIDSVVIGKDQEVKLQPGQVLHMVNELYPYIVEFEEEAKNPGL ETHRKRKRSGNSDSIERDAAQEAEAGTGLEPGSNSGQCSVPLK KGKDAPIKKESLGHWSQGLKISMQDPKMQVYKDEQVVVIKDKY PKARYHWLVLPWTSISSLKAVAR\EHLELLKHMHTVGEKVIVD FAGSSKLRFRLGYHAIPSMSHVHLHVISQDFDSPCLKNKKHWN SFNTEYFLESQAVIEMVQEAGRVTVRDGMPELLKLPLRCHECQ QLLPSIPQLKEHLRKHWTQ

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524	1263	2067	198	DMSDTSESGAGLTRFQAEASEKDSSSMMQTLLTVTQNVEVPET PKASKALEVSEDVKVSKASGVSKATEVSKTPEAREAPATQASS TTQLTDTQVLAAENKSLAADTKKQNADPQAVTMPATETKKVSH VADTKVNTKAQETEAAPSQAPADEPEPESAAAQSQENQDTRPK VKAKKARKVKHLDGEEDGSSDQSQASGTTGGRRVSKALMASMA RRASRGPIAFWARRASRTRLACFGPGEPLLSPWRSP\KARRQR GFAVRVAKFQ\SSQEPEAPPPW\DVALLQGRAN\DLVKYLLAK DQTKIPIKRS\DMLKDIIKEYTDVYPEII\ERAGYSLE\KVFG IQLKEIDKNDHLYILLSTLEPTDAGILGTTKDSPKLGLLMVLL SIIF\MNGNRS\SEAVIWEVLR/RSLGLRLGIHHS\LLGDVK\ KLITDEV\VKQKYL\DYARVPHSNSP\EYEFFWG\LRSYYEDQ QR*KSFKFACK\VQK\KDPK\EWAAQSPPGKAR/ERMEAD\LK AAS*GSPWKPRLRAEIKARMGIGLGSENAAGPCNWDEADIGPW AKARIQAGAEAKAKAQESGSASTGASTSTNNSASASASTSGGF SAGASLTATLTFGLFAGLGGAGASTSGSSGACGFSYK
525	1264	1	1397	ARPPVCTGSTMSLTVVSMACVGFFLLQGAWPLMGGQDKPFLSA RPSTVVPRGGHVALQCHYRRGFNNFMLYKEDRSHVPIFHGRIF QESFIMGPVTPAHAGTYRCRGSRPHSLTGWSAPSNPLVIMVTG NHRKPSLLAHPGPLLKSGETVILQCWSDIMFEHFFLHKEGISK DPSRLVGQIHDGVSKANFSIGPMMLALAGTYRCYGSVTHTPYQ LSAPSDPLDIVVTGPYEKPSLSAQPGPKVQAGESVTLSCSSRS SYDMYHLSREGGAHERRLPAVRKVNRTFQADFPLGPATHGGTY RCFGSFRHSPYEWSDPSDPLLVSVTGNPSSSWPSPTEPSSKSG NLRHLHILIGTSVVKIPFTILLFFLLHRWCSNKK\NAAVMDQE PAGNR\VNSEDSDEQDHQEVSYP*LEHCVFTQRKITRPSQRPK TPPTDTSMYIELPNAEPRSKVVFCPRAPQSGLEGIF

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526	1265	6657	988	LHNLRERYFSGLIYTYSGLFCVVVNPYKHLPIYSEKIVDMYKG KKRHEMPPHIYAIADTAYRSMLQDREDQSILCTGESGAGKTEN TKKVIQYLAVVASSHKGKKDTSITGELEKQLLQANPILEAFGN AKTVKNDNSSRFGKFIRINFDVTGYIVGANIETYLLEKSRAIR QARDERTFHIFYYMIAGAKEKMRSDLLLEGFNNYTFLSNGFVP IPAAQDDEMFQETVEAMAIMGFSEEEQLSILKVVSSVLQLGNI VFKKERNTDQASMPDNTAAQKVCHLMGINVTDFTRSILTPRIK VGRDVVQKAQTKEQADFAVEALAKATYERLFRWILTRVNKALD KTHRQGASFLGILDIAGFEIFEVNSFEQLCINYTNEKLQQLFN HTMFIL\EQEEYQREGIEWNFIDFGLDLQPCIELIERPNNPPG VLALLDEECWFPKATDKSFVEKLCTEQGSHPKFQKPKQLKDKT EFSIIHYAGKVDYNASAWLTKNMDPLNDNVTSLLNASSDKFVA DLWKDVDRIVGLDQMAKMTESSLPSASKTKKGMFRTVGQLYKE QLGKLMTTLRNTTPNFVRCIIPNHEKRSGKLDAFLVLEQLRCN GVLEGIRICRQGFPNRIVFQEFRQRYEILAANAIPKGFMDGKQ ACILMIKALELDPNLYRIGQSKIFFRTGVLAHLEEERDLKITD VIMAFQAMCRGYLARKAFAKRQQQLTAMKVIQRNCAAYIKLRN WQWCRLFTKV*PLLQVTRQE*EMQAKEDELQKTKERQQKAENE LKELEQKHSQLTEEKNLLQEQLQAETELYAEAEEMRVRLAAKK QELEEILHEMEARLEEEEDRGQQLQAERKKMAQQMLDLEEQLE EEEAARQKLQLEKVTAEAKIKKLEDEILVMDDQNNKLSKERKL LEERISDLTTNLAEEEEKAKNLTKLKNKHESMISELEVRLKKE EKSRQELEKLKRKLEGDASDFHEQIADLQAQIAELKMQLAKKE EELQAALARLDDEIAQKNNALKKIRELEGHISDLQEDLDSERA ARNKAEKQKRDLGEELEALKTELEDTLDSTATQQELRAKREQE VTVLKR\ALNEETRSHEAQVQEMRQKHAQAVQSLTEQLEQ*K RAKANLDKNKQTLEKENTD\LAGELRVLGQA\KQEVEHRMKKL QAQVQELQSKCSDGERARAELNDKVHK\LQNEVESVTG\MLNE AEGKAIKLAKDVASLSSQL\QDTQELLQEESRQKLNVST\SLR \QLEEERNSLQDQLDEEMEAKQNLERHISTLNIQLSDSKKKLQ DFASTVEALEEGKKRFQKEIENLTQQYEEKAAAYDKLEKTKNR LQQELDDLVVDLDNQRQLVSNLEKKQRKFDQLLAEEKNISSKY ADERDRVEAEAREKETKALSL\ARALEEALEAKEELERTNKML KA\EMGRPGSASKD\DVGQELSHDL\EKSK\RALGDPRLEEMK T\QLEELGRTELASPRRDA\KLRLEVNMQAPSRASFER\DLQA RTEQNE\ESRR\HLQRQLHEYETELEDERKQRALAAAAKIKLG WDPVRTLDL*ADSAIKGRGGKAIKQLRKLQAQMKDFQRELEDA \RASRDEIF\ATA\KENEKKAKSLEA\DLMQLQE\DLAAAEEG RKQ\ADLE\KEELAEEL\ASSLSGRNALQDEKRRLEARIAQLE EELEEEQGNMEAMSDRVRKATQQAEQLSNELATERSTAQKNES ARQQLERQNKELRSKLHEMEGAVKSKFKSTIAALEAKIAQLEE QVEQEAREKQAATKSLKQKDKKLKEILLQVEDERKMAEQYKEQ AEKGNARVKQLKRQLEEAEEESQRINANRRKLQRELDEATESN EAMGREVNALKSKLRRGNETSFVPSRRSGGRRVIENADGSEEE TDTRDADFNGTKASE

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527	1266	1	775	KLHFAKSLNSELSCSTREAMQDEDGYITLNIKTRKPALVSVGP ASSSWWRVMALILLILCVGMVVGLVALGIWSVMQRNYLQDENE NRTGTLQQLAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYG DSCYGFFRHNLTWEESKQYCTDMNATLLKIDNRNIVEYIKAR\ THLIRWVGLSRQKSNEVWKWEDGSVISENMFEFLEDGKGNMNC AYFHNGKMHPTFCENKHYL\MCE\RKAGHDPRWTQLPLMPKRW TG
528	1267	1053	424	NQGLRDVGLCRTCLVNKIFASSILGKSHHHSLVSINQGHNAPW KAAGS\LPLKAAYC\QGFSPCDCLKYG\SWDEKDLMVPQPDTH KGSVLRWISKRGKPLAVEMEEGHCL\CLPLGTECLGVKP\IVH LFNSEMGEK\RPVAG\ARHVGSSAALLFFTPLRCLGGEKHKSG LRARPGIVPSLELNYDIDSFAHMFF/SVDLLLIITLLSYYIPF C
529	1268	1435	1560	MWWRLAPTQAIWRAAGCCMRFSRRRSTCCCLASCIFLLYKIVR GDQPAAKRRQRRRRAAPSAPPQAARLHPPPKLRRFDGVQDPAP YSWAINGKVFDVTQRPANFLRGPRGPETLSDWESQFTFKYHHV GKLLKEGEEPTVYSDEEEPKDESARKND*
530	1269	705	166	GPRMAKFLSQDQINEYKECFSLYDKQQRGKIKATDLMVAMRCL GASPTPGEVQRHLQTHGIDGNGELDFSTFLTIMHMQIKQEDPK KEILLAMLMVDKEKKGYVMASDLRSKLTSLGEKLTHKEV\DDL FRE\ADIEPNGKVKYDEFIHKI/TLLPGRDLLKEENGRASPGP ENLEQLIFL
531	1270	25	1396	ADPHTTVIRFFPAASATKRVLPPVLRVSSPRTWNPNVPESPRI PAPRLPKRMSGAPTAGAALMLCAATAVLLSAQGGPVQSKSPRF ASWDEMNVLAHGLLQLGQGLREHAERTRSQLSALERRLSACGS ACQGTEGSTDLPLAPESRVDPEVLHSLQTQLKAQNSRIQQLFH KVAQQQRHLEKQHLRIQHLQSQFGLLDHKHLDHEVAKPARRKR LPEMAQPVDPAHNVSRLHRLPRDCQELFQVGERQSGLFEIQPQ GSPPFLVNCKMTSDGGWTVIQRRHDGSVDFNRPWEAYKAGFGD PHGEFWLGLEKVHSITGDRNSRLAVQLRDWDGNAELLQFSVHL GGEDTAYSLQLTAPVAGQLGATTVPPSGLSVPFSTWDQDHDLR RDKNCAKSLSGGWWFGTCSHSNLNGQYFRSIPQQRQKLKKGIF WKTWRGRYYPLQATTMLIQPMAAEAAS
532	1271	1276	90	ALDFGDSCQWPRPQDTMKQLPVLEPGDKPRKATWYTLTVPGDS PCARVGHSCSYLPPVGNAKRGKVFIVGGANPNRSFSDVHTMDL GKHQWDLDTCKGLLPRYEHASFIPSCTPDRIWVFGGANQSGNR NCLQVLNPETRTWTTPEVTSPPPSPRTFHTSSAAIGNQLYVFG GGERGAQPVQDTKLHVFDANTLTWSQPETLGNPPSPRHGHVMV AAGTKLFIHGGLAGDRFYDDLHCIDISDMKWQKLNPTGAA\PA GCAS/HTPAVAMGK\HVYI\FGGMTPAGAPGTQCTQYHTEEQH WDPCLKF\DTPSYPPGTIGTHSHVVSFPW\PVTCASEKEDS\N SLTLNHEAEKEDSADKVMSHSGDSHEESQTATLLCLVFGGMNT EGEIYDDCIVTVVD

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533	1272	1169	639	GFSIGKATDRMDAFRKAKNRAVHHLHYIERYEDHTIFHDISLR FKRTHIKMKKQPKGYGLRCHRAIITICRLIGIKDMYAKVSGSI NMLSLTQGLFRGLSRQETHQQLADKKGLHVVEIREECGPLPIV VASPRGPLRKDPEPEDEVPDVKLDWEDVKTAQGMKRSVWSNLK RAAT
534	1273	25	1396	ADPHTTVIRFFPAASATKRVLPPVLRVSSPRTWNPNVPESPRI PAPRLPKRMSGAPTAGAALMLCAATAVLLSAQGGPVQSKSPRF ASWDEMNVLAHGLLQLGQGLREHAERTRSQLSALERRLSACGS ACQGTEGSTDLPLAPESRVDPEVLHSLQTQLKAQNSRIQQLFH KVAQQQRHLEKQHLRIQHLQSQFGLLDHKHLDHEVAKPARRKR LPEMAQPVDPAHNVSRLHRLPRDCQELFQVGERQSGLFEIQPQ GSPPFLVNCKMTSDGGWTVIQRRHDGSVDFNRPWEAYKAGFGD PHGEFWLGLEKVHSITGDRNSRLAVQLRDWDGNAELLQFSVHL GGEDTAYSLQLTAPVAGQLGATTVPPSGLSVPFSTWDQDHDLR RDKNCAKSLSGGWWFGTCSHSNLNGQYFRSIPQQRQKLKKGIF WKTWRGRYYPLQATTMLIQPMAAEAAS
535	1274	23	1102	TLRSRPAGEAGYLGWDPEQAGEGSALSRPGAMAALMTPGTGAP PAPGDFSGEGSQGLPDPSPEPKQLPELIRMKRDGGRLSEADIR GFVAAVVNGSAQGAQIGAWGGLGVPDPDWEVSPRDFGSLGVRR CPTTSTGPRVPHRCGLPPSRVPPHTRG\MLMAIRLRGMDLEET SVLTQALAQSGQQLEWPEAWRQQLVDKHSTGGVGDKVSLVLAP ALAACGCKVINHLLSRREPIPHMQQPVHPQAAPNLKPGPKPPR PYQGFSPPCSPAQFSPPRSPAQRLGPLWLQTRPLGAGKRSTDG IQTPFPLGPQTAPPREELRTSLPLPQALFPQGQVPTSSPTDTS QPRKLPFHSLTSWAPL
536	1275	3	439	RALRELRERVTHGLAEAGRDREDVSTELYRALEAVRLQNSEGS CEPCPTSWLPFGGSCYYFSVPKTTWAEAQGHCADASAHLA/IV GGLGEQDFLSRDTSALEYWIGRRAVQHLRKVQGYSWVDGVPLS FR*/WEG/HPGETWGPQVRL
537	1276	1	564	RWPRSWPPRAGAARGAAEAAMVGALCGCWFRLGGARPLIPLGP TVVQTSMSRSQVALLGLSLLLMLLLYVGLPGPPEQTSCLWGDP NVTVLAGLTPGNSPIFYREVLPLNQAHRVEV\CCFMERPLTLT RGSSWAHCSYCHRGATGPWPLTFQVLGTRHLQRRQAQRQGGQR CWSGRCGTWRYRMPCW

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538	1277	102	1549	QENQLEKKMKFLIFAFFGGVHLLSLCSGKAICKNGISKRTFEE IKEEIASCGDVAKAIINLAVYGKAQNRSYERLALLVDTVGPRL SGSKNLEKAIQIMYQNLQQDGLEKVHLEPVRIPHWERGEESAV MLEPRIHKIAILGLGSSIGTPPEGITAEVLVVTSFDELQRRAS EARGKIVVYNQPYINYSRTVQYRTQGAVEAAKVGALASLIRSV ASFSIYSPHTGIQEYQDGVPKIPTACITVEDAEMMSRMASHGI KIVIQLKMGAKTYPDTDSFNTVAEITGSKYPEQVVLVSGHLDS WDVGQGAMDDGGGAFISWEALSLIKDLGLRPKRTLRLVLWTAE EQGGVGAFQYYQLHKVNISNYSLVMESDAGTFLPTGLQFTGSE KARAIMEEVMSLLQPLNITQVLSHGEGTDINFWIQAGVPGASL LDDLYKYFFFHHSHGDTMTVHGIQTQMNV\AAAV\WAVVSYV\ VADMEEMLPRS
539	1278	2438	1148	TKPRKRRHQPASQRQRPWSSDSTGDLLARGKGRKEENKGSDRV SLAPPSLRRPMMCQSEARQGPELRAAKWLHFPQLALRRRLGQL SCMSRPALKLRSWPLTVLYYLLPFGALRPLSRVGWRPVSRVAL YKSVPTRLLSRAWGRLNQVELPHWLRRPVYSLYIWTFGVNMKE AAVEDLHHYRNLSEFFRRKLKPQARPVCGLHSVISPSDGRILN FGQVKNCEVEQVKGVTYSLESFLGPRMCTEDLPFPPAASCDSF KNQLVTREGNELYHCVIYLAPGDYHCFHSPTDWTVSHRRHFPG SLMSVNPGMARWIKELFCHNERVVLTGDWKHGFFSLTAVGAT\ NWGSIRIYFDRDLHTNSPRHSKGSYNDFSFVTHTNREGVPMRK GEHLGEFNLGSTIVLIFEAPKDFNFQLKTGQKI\RFGEALGSL
540	1279	3	1911	LPERAFGPRTPRAPRRRRRRLLLSPPPRPPPPLDREPRAPGPW LCPSRAGTAQDPARIRERRGRVAGGAAGPAMELRARGWWLLCA AAALVACARGDPASKSRSCGEVRQIYGAKGFSSS\DVPQAEIS GEHLRICPQGYTCCTSEMEENLANRSHAELETALRDSSRVLQA MLATQLRSFDDHFQHLLNDSERTLQATFPGAFGELYTQNARAF RDLYSELRLYYRGANLHLEETLAEFWARLLERLFKQLHPQLLL PDDYLDCLGKQAEALRPF\GEAP\RELRLRAT\RA\FVAAR\S FVQGLGVAS\DVVRKVAQVPLG\PEC\SRAVIEAGSYC/ALHC VGVPGARPCPDYCRNVLKGCLANQADLDAEWRNLLDSMVLITD KFWGTSGVESVIGSVHTWLAEAINALQDNRDTLTAKVIQGCGN PKVNPQGPGPEEKRRRGKLAPRERPPSGTLEKLVSEAKAQLRD VQDFWISLPGTLCSEKMALSTASDDRCWNGMARGRYLPEVMGD GLANQINNPEVEVDITKPDMTIRQQIMQLKIMTNRLRSAYNGN DVDFQDASDDGSGSGSGDGCLDDLCGRKVSRKSSSSRTPLTHA LPGLSEQEGQKTSAASCPQPPTFLLPLLLFLALTVARPRWR
541	1280	590	189	ATELTRAGMEASALTKSA\VTSVAKVVR\VASGSAVVLPLARI ATSCD*RVGGP/VQAVPMVL\SAMGLQLRAGIASSSIAAKMMS AAAIA\NGGGVSPGQPLWLLLQSLGATGL\SGLTKFILGSIGS AIA\AVIARFY

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542	1281	41	1415	TNGRNLLHHWILGVCGMHPHHQETLKKNRVVLAKQLLLSELLE HLLEKDIITLEMRELIQAKVGSFSQNVELLNLLPKRGPQAFDA FCEALRETKQGHLEDMLLTTLSGLQHVLPPLSCDYDLSLPFPV CESCPLYKKLRLSTDTVEHSLDNKDGPVCLQVKPCTPEFYQTH FQLAYRLQSRPRGLALVLSNVHFTGEKELEFRSGGDVDHSTLV TLFKLLGYDVHVLCDQTAQEMQEKLQNFAQLPAHRVTDSCIVA LLSHGVEGAIYGVDGKLLQLQEVFQLFDNANCPSLQNKPKMFF IQACRGGAIGSLGHLLLFTAATASLAL\ETDRGVDQQDGKNHA GSPGCEESDAGKEKLPKMRLPTRSDMICGYACLKGTAAMRNTK RGSWYIEALAQVFSERACDMHVADMLVKVNALIKDREGYAPGT EFHRCKEMSEYCSTLCRHLYLFPGHPPT
543	1282	862	275	VRGKEVMAALCRTRAVAAESHFLRVFLFFRPFRGVGTESGSES GSSNAKEPKTRAGGFASALERHSELLQKVEPLQKGSPKNVESF ASMLRHSPLTQMGPAKDKLVIGRIFHIVENDL\YIDFGGKFHC VCRRPEVDGEKY\QKGTRVR\LRLLDLELTSRFLGATTD\TTV LEANAVLLGIQESKDSRSKEEHLEKYI

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544	1283	2	4503	IPGASPAPRRAAPLRLGLRLASGWARAPGGVSPVPGPGMGGDA PTMARAQALVLELTFQLCAPETETPEVGCTFEEGSDPAVPCEY SQAQYDDFQWEQVRIHPGTRAPADLPHGSYLMVNTSQHAPGQR AHVIFQSLSENDTHCVQFSYFLYSRDGHSPGTLGVYVRVNGGP LGSAVWNMTGSHGRQWHQAELAVSTFWPNEYQVLFEALISPDR RGYMGLDDILLLSYPCAKAPHFSRLGDVEVNAGQNASFQCMAA GRAAEAERFLLQRQSGALVPAAGVRHISHRRFLATFPLAAVSR AEQDLYRCVSQAPRGRGTSLNFAEFMV/KEPPTPIAPPQLLRA GPTYLIIQLNTNSIIGDGPIVRKEIEYRMARGPWAEVHAVSLQ TYKLWHLDPDTEYEISVLLTRPGDGGTGRPGPPLISRTKCAEP MRAPKGLAFAEIQARQLTLQWEPLGYNVTRCHTYTVSLCYHYT LGSSHNQTI\RECVKTEQGVSRYTMKNLLPYRNVHVRLVLTNP EGRKEGKEVTFQTDEDVPSGIAAESLTFTPLEDMIFLKWEEPQ EPNGLITQYEISYQSIESSDPAVNVPGPRRTISKLRNETYHVF SNLHPGTTYLFSVRARTGKGFGQAALTEITTNISAPSFDYADM PSPLGESENTITVLLRPAQGRGAPISVYQVIVEEEQGSRRLRR EPGGQDCFPVPLTFEAALARGLVDYFGAELAASSLPEAMPFTV GDNKTYRGFWNPPLEPRKAYLIYFQAASHLKGETRLNCIRIAR KAACKESKRPLEVSQRSEEMGLILGICAGGLAVLILLLGAIIV IIRKGRDHYAYSYYPKPVNMTKATVNYRQEKTHMMSAVDRSFT DQSTLQEDERLGLSFMDTHGYSTRGDQRSGGVTEASSLLGGSP RRPCGRKGSPYHTGQLHPAVRVADLLQHINQMKTAEGYGFKQE YESFFEGWDATKKKDKVKGSRQEPMPAYDRHRVKLHPMLGDPN ADYINANYIDIRINREGYHRSNHFIATQGPKPEMVYDFWRMVW QEHCSSIVMITKLVEVGRVKCSRYWPEDSDTYGDIKIMLVKTE TLAEYVVRTFALERRGYSARHEVRQFHFTAWPEHGVPYHATGL LAFIRRVKASTPPDAGPIVIHCSAGTGRTGCYIVLDVMLDMAE CEGVVDIYNCVKTLCSRRVNMIQTEEQYIFIHDAILEACLCGE TTIPVSEFKATYKEMIRIDPQSNSSQLREEFQTLNSVTPPLDV EECSIALLPRNRDKNRSMDVLPPDRCLPFLISTDGDSNNYINA ALTDSYTRSAAFIVTLHPLQSTTPDFWGLVYDYGCTSIVMLNQ LNQSNSAWPCLQYWPEPGRQQYGLMEVEFMSGTADEDLVARVF RVQNISRLQEGHLLVRHFQFLRWSAYRDTPDSKKAFLHLLAEG DKWQAESGDGRTIVHCLNGGGRSGTFCA\CATVLEMIRCHNLV DVFFAAKTLRNYKPNMVETMDQYHFCYDVALEYLEGLESR

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545	1284	2443	1152	TKPRKRRHQPASQRQRPWSSDSTGDLLARGKGRKEENKGSDRV SLAPPSLRRPMMCQSEARQGPELRAAKWLHFPQLALRRRLGQL SCMSRPALKLRSWPLTVLYYLLPFGALRPLSRVGWRPVSRVAL YKSVPTRLLSRAWGRLNQVELPHWLRRPVYSLYIWTFGVNMKE AAVEDLHHYRNLSEFFRRKLKPQARPVCGLHSVISPSDGRILN FGQVKNCEVEQVKGVTYSLESFLGPRMCTEDLPFPPAASCDSF KNQLVTREGNELYHCVIYLAPGDYHCFHSPTDWTVSHRRHFPG SLMSVNPGMARWIKELFCHNERVVLTGDWKHGFFSLTAVGAT\ NWGSIRIYFDRDLHTNSPRHSKGSYNDFSFVTHTNREGVPMAL RGEHLG/QSFNLGSTIVLIFEAPKDFNFQLKTGQKIRFGEALG SL
546	1285	185	3057	AELGLFGSLRFSSLLHFPPRPRSPASACGPGEGRMERGLPLLC AVLALVLAPAGAFRNDKCGDTIKIESPGYLTSPGYPHSYHPSE KCEWLIQAPDPYQRIMINFNPHFDLEDRDCKYDYVEVFDGENE NGHFRGKFCGKIAPPPVVSSGPFLFIKFVSDYETHGAGFSIRY EIFKRGPECSQNYTTPSGVIKSPGFPEKYPNSLECTYI\VFAP KMSEIIL\DFESFDLEPDSNPPGGMFCRYDRLEIWDGFPDVGP HIGRYCGQKTPGRIRSSSGILSMVFYTDSAIAKEGFSANYSVL QSSVSEDFKCMEALGMESGEIHSDQITASSQYSTNWSAERSRL NYPENGWTPGEDSYREWIQVDLGLLRFVTAVGTQGAISKETKK KYYVKTYKIDVSSNGEDWITIKEGNKPVLFQGNTNPTDVVVAV FPKPLITRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGM VSGLISDSQITSSNQGDRNWMPENIRLVTSRSGWALPPAPHSY INEWLQIDLGEEKIVRGIIIQGGKHRENKVFMRKFKIGYSNNG SDWKMIMDDSKRKAKSFEGNNNYDTPELRTFPALSTRFIRIYP ERATHGGLGLRMELLGCEVEAPTAGPTTPNGNLVDECDDDQAN CHSGTGDDFQLTGGTTVLATEKPTVIDSTIQSEFPTYGFNCEF GWGSHKTFCHWEHDNHVQLKWSVLTSKTGPIQDHTGDGNFIYS QADENQKGKVARLVSPVVYSQNSAHCMTFWYHMSGSHVGTLRV KLRYQKPEEYDQLVWMAIGHQGDHWKEGRVLLHKSLKLYQVIF EGEIGKGNLGGIAVDDISINNHISQEDCAKPADLDKKNPEIKI DETGSTPGYEGEGEGDKNISRKPGNVLKTLEPILITIIAMSAL GVLLGAVCGVVLYCACWHNGMSERNLSALENYNFELVDGVKLK KDKLNTQSTYSEA
547	1286	3	521	HEGSALTWASHYQERLNSEQSCLNEWTAMADLESLRPPSAEPG GSVCGGEGLGGGEGRIMQWGAWWRGERAP*LRGSAPRSSEQEQ MEQAIRAELWKVLDVSDLESVTSKEIRQALELRLGLPLQ/PVP *LHRQPDAAAGGTAGPSLPHLPPPLPGLRVERSKPGGAAEEQV GL
548	1287	1742	1200	MAALDLRAELDSLVLQLLGDLEELEGKRTVLNARVEEGWLSLA KARYAMGAKSVGPLQYASHMEPQVCLHASEAQEGLQKFKVVRA GVHAPEEVGPREAGLRRRKGPTKTPEPESSEAPQDPLNWFGIL VPHSLRQAQASFRDGLQLAADIASLQNRIDWGRSQLRGLQEKL KQLEPGAA*

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
549	1288	1	649	HSDVGAATAVLPLLTAVLGVTVVTRRDTEGPGRAALVHLTGSP RQKVGTSGREGLPGLGASCAESELERETQEPRSRGRCIFGAAR WRQVPLASPQRPFLLSPGPRLHRMGLPVSWAPPALWVLGCCAL LLSLWALCTACRRPEDAVAPRKRARRQRARLQGSATAAEAVSA KLSRGPGWGPQGTDQPSSPPVPTEADPPLLPQQVGHQTARAAP G
550	1289	433	632	LTGPGQRLAGTTEGPRRCRGSSQAPTPTWKLVDTRLCAAAPWL ASRAPGHYSQMLLVN*PCRKDWLVSKWMRTPVCGQSPAMTDRP RSEAGRDHRRAKALPGLIPGSNPNLEACGHQALCSSSVASVQG PWPLLPNASSPPTPGQPQP
551	1290	102	612	KHRLCSLEQLMTLISAAREYEIEFIYAISPGLDITFSNPKEVS TLKRKLDQVSQFGCRSFALLFDDIDHNMCAADKEVFSSFAHAQ VSITNEIYQYLGEPETFLFCPT/EYCI*WLYI*LVFLEYITYK GPWAPFSLHFPPPLVCKSRNLFLEDIFQDPKLEKF*ELINDN
552	1291	269	565	TSALTQGLERIPDQLGYLVLSEGAVLASSGDLENDEQAASAIS ELVSTACGFRLHRGMNVPFKRLSVVFGEHTLLVTVSGQRVFVV KRQNRGREPIDV
553	1292	660	233	AKRAERTSRLQGLQHPSPPYPPATLGVTPGQDRTLQLQHQCPA GRKSRKKKSKATQLSPEDRVEDALPPSKAPSRTRRAKRDLPKR TATQRPEGTSLQQDPEAPTVPKKGRRKGRQAASGHCRPRKVKA DIPSLEPEGTSAS
554	1293	590	323	RKSSWLGAVAHACNPSSLGGPGRQITRSGVRDQPGQYGETPSL LKIQTLAGRGGACL*SHILRRLRQKNRLNLGGRGCSELRSRHC APA
555	1294	1	242	AWNSARGAVSPLWVPGCFLTLSVTWIGAAPLILSRIVGGWECE KHSQPWQVLVASRGRAVCGGVLVHPQWVLTAAHCIRK
556	1295	1074	230	AEMADDLGDEWWENQPTGAGSSPEASDGEGEGDTEVMQQETVP VPVPSEKTKQPKECFLIQPKERKENTTKTRKRRKKKITDVLAK SEPKPGLPEDLQKLMKDYYSSRRLVIELEELNLPDSCFLKAND LTHSLSSYLKEICPKWVKLRKNHSEKKSVLMLIICSSAVRALE LIRSMTAFRGDGKVIKLFAKHIKVQAQVKLLEKRVVHLGVGTP GRIKELVKQGGLNLSPLKFLVFDWNWRDQKLRRMMDIPEIRKE VFELLEMGVLSLCKSESLKLGLF
557	1296	929	289	RPGTAIWVVECEHGRPIAESEGQEGRGHSPPGPCSVAGFLRGR LGRNLEIMGSTWGSPGWVRLALCLTGLVLSLYALHVKAARARD RDYRALCDVGTAISCSRVFSSRWGRGFGLVEHVLGQDSILNQS NSIFGCIFYTLQLLLGCLRTRWASVLMLLSSLVSLAGSVYLAW ILFFVLYDFCIVCITTYAINVSLMWLSFRKVQEPQGKAKRH

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558	1297	2	1063	ESPAPPAFRPAMAAVALMPPPLLLLLLLASPPAASAPSARDPF APQLGDTQNCQLRCRDRDLGPQPSQAGLEGASESPYDRAVLIS ACERGCRLFSICRFVARSSKPNATQTECEAACVEAYVKEAEQQ ACSHGCWSQPAEPEPEQKRKVLEAPSGALSLLDLFSTLCNDLV NSAQGFVSSTWTYYLQTDNGKVVVFQTQPIVESLGFQGGRLQR VEVTWRGSHPEALEVHVDPVGPLDKVRKAKIRVKTSSKAKVES EEPQDNDFLSCMSRRSGLPRWILACCLFLSVLVMLWLSCSTLV TAPGQHLKFQPLTLEQHKGFMMEPDWPLYPPPSHACEDSLPPY KLKLDLTKL
559	1298	2	485	FPELGTSLSAMRFLAATFLLLALSTAAQAEPVQFKDCGSVDGV IKEVNVSPCPTQPCQLSKGQSYSVNVTFTSNIQSKSSKAVVHG ILMGVPVPFPIPEPDGCKSGINCPIQKDKTYSYLNKLPVKSEY PSIKLVVEWQLQDDKNQSLFCWEIPVQIVSHL
560	1299	1304	919	APETFRCVWRLQGLTFIAFTELQAKVIDTQQKVKLADIQIEQL NRTKKHAHLTDTEIMTLVDETNMYEGVGRMFILQSKEAIHSQL LEKQKIAEEKIKELEQKKSYLERSVKEAEDNIREMLMARRAQ
561	1300	3	799	HSLLLGTRVRDASSKIQGEYTLTLRKGGNNKLSRVFHRDGHYG FSEPLTFCSVVDLINHYRHESLAQYNAKLDTRLLYPVSKYQQV RAGLGAREGSTWLAPGLSFLGRPDQAMHLPSFRHVSP\DQIVK EDSVEAVGAQLKVYHQQYQDKSREYDQLYEEYTRTSQELQMKR TAIEAFNETIKIFEEQGQTQEKCSKEYLERFRREGN/QTKEMQ RILLNSERLKSRIA\EIHESPHRSWEQQLLVPRASDNKRD/ID KPH*TSLKPDL
562	1301	1772	301	AAAAAGRGRSSGRRRRRRPGALFASLGVLLGPRPPPGIPRTRA CSMGGVGEPGPREGPAQPGAPLPTFCWEQIRAHDQPGDKWLVI ERRVYDISRWAQRHPGGSRLIGHHGAEDATDAFRAFHQDLNFV RKFLQPLLIGELAPEEPSQDGPLNAQLVEDFRALHQAAEDMKL FDASPTFFAFLLGHILAMEVLAWLLIYLLGPGWVPSALAAFIL AISQAQSWCLQHDLGHASIFKKSWWNHVAQKFVMGQLKGFSAH WWNFRHFQHHAKPNIFHKDPDVTVAPVFLLGESSVEYGKKKRR YLPYNQQHLYFFLIGPPLLTLVNFEVENLAYMLVCMQWADLLW AASFYARFFLSYLPFYGVPGVLLFFVAVRVLESHWFVWITQMN HIPKEIGHEKHRDWVSSQLAATCNVEPSLFTNWFSGHLNFQIE HHLFPRMPRHNYSRVAPLVKSLCAKHGLSYEVKPFLTALVDIV RSLKKSGDIWLDAYLHQ
563	1302	424	93	KSRATRLRESAEMTGFLLPPASRGTRRSCSRSRKRQTRRRRNP SSFVASCPTLLPFACVPGASPTTLAFPPVVLTGPSTDGIPFAL SLQRVPFVLPSPQVASLPLGHSRG
564	1303	1	414	IQYRSDLELHSITMKKSGVLFLLGIILLVLIGVQGTPVVRKGR CSCISTNQGTIHLQSLKDLKQFAPSPSCEKIEIIATLKNGVQT CLNPDSADVKELIKKWEKQVSQKKKQKNGKKHQKKKVLKVRKS QRSRQKKTT

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565	1304	7	3007	IPGSTISCRGCCGKWPVQEADPPRAALRGRFPALLTRHCPSPR AEKEKRSLRRCGCRPLLVELAGPAGQAVEVLPHFESLGKQEKI PNKMSAFRNHCPHLDSVGEITKEDLIQKSLGTCQDCKVQGPNL WACLENRCSYVGCGESQVDHSTIHSQETKHYLTVNLTTLRVWC YACSKEVFLDRKLGTQPSLPHVRQPHQIQENSVQDFKIPSNTT LKTPLVAVFDDLDIEADEEDELRARGLTGLKNIGNTCYMNAAL QALSNCPPLTQFFLDCGGLARTDKKPAICKSYLKLMTELWYKS RPGSVVPTTLFQGIKTVNPTFRGYSQQDAQEFLRCLMDLLHEE LKEQVMEVEEDPQTITTEETMEEDKSQSDVDFQSCESCSNSDR AENENGSRCFSEDNNETTMLIQDDENNSEMSKDWQKEKMCNKI NKVNSEGEFDKDRDSISETVDLNNQETVKVQIHSRASEYITDV HSNDLSTPQILPSNEGVNPRLSASPPKSGNLWPGLAPPHKKAQ SASPKRKKQHKKYRSVISDIFDGTIISSVQCLTCDRVSVTLET FQDLSLPIPGKEDLAKLHSSSHPTSIVKAGSCGEAYAPQGWIA FFMEYVKRFVVSCVPSWFWGPVVTLQDCLAAFFARDELKGDNM YSCEKCKKLRNGVKFCKVQNFPEILCIHLKRFRHELMFSTKIS THVSFPLEGLDLQPFLAKDSPAQIVTYDLLSVICHHGTASSGH YIAYCRNNLNNLWYEFDDQSVTEVSESTVQNAEAYVLFYRKSS EEAQKERRRISNLLNIMEPSLLQFYISRQWLNKFKTFAEPGPI SNNDFLCIHGGVPPRKAGYIEDLVLMLPQNIWDNLYSRYGGGP AVNHLYICHTCQIEAEKIEKRRKTELEIFIRLNRAFQKEDSPA TFYCISMQWFREWESFVKGKDGDPPGPIDNTKIAVTKCGNVML RQGADSGQISEETWNFLQSIYGGGPEVILRPPVVHVDPDILQA EEKIEVETRSL
566	1305	28	450	SPSAAGGLAWVSLALGSGSRGRDHSGSGVGTAMAGALVRKAAD YVRSKDFRDYLMSTHFWGPVANWGLPIAAINDMKKSPEIISGR MTFALCCYSLTFMRFAYKVQPRNWLLFACHATNEVAQLIQGGR LIKHEMTKTASA
567	1306	133	1292	LGSRQAAGTMRGQRSLLLGPARLCLRLLLLLGYRRRCPPLLRG LVQRWRYGKVCLRSLLYNSFGGSDTAVDAAFEPVYWLVDNVIR WFGVVFVVLVIVLTGSIVAIAYLCVLPLILRTYSVPRLCWHFF YSHWNLILIVFHYYQAITTPPGYPPQGRNDIATVSICKKCIYP KPARTHHCSICNRCVLKMDHHCPWLNNCVGHYNHRYFFSFCFF MTLGCVYCSYGSWDLFREAYAAIEKMKQLDKNKLQAVANQTYH QTPPPTFSFRERMTHKSLVYLWFLCSSVALALGALTVWHAVLI SRGETSIERHINKKERRRLQAKGRVFRNPYNYGCLDNWKVFLG VDTGRHWLTRVLLPSSHLPHGNGMSWEPPPWVTAHSASVMAV
568	1307	66	962	ATRRRAAEAGMAAVLQRVERLSNRVVRVLGCNPGPMTLQGTNT YLVGTGPRRILIDTGEPAIPEYISCLKQALTEFNTAIQEIVVT HWHRDHSGGIGDICKSINNDTTYCIKKLPRNPQREEIIGNGEQ QYVYLKDGDVIKTEGATLRVLYTPGHTDDHMALLLEEENAIFS GDCILGEGTTVFEDLYDYMNSLKELLKIKADIIYPGHGPVIHN AEAKIQQYISHRNIREQQILTLFRENFEKSFTVMELVKIIYKN TPENLHEMAKHNLLLHLKKLEKEGKIFSNTDPDKKWKAHL

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569	1308	96	1017	ELHRAGQVAGGARRSRRESMELERIVSAALLAFVQTHLPEADL SGLDEVIFSYVLGVLEDLGPSGPSEENFDMEAFTEMMEAYVPG FAHIPRGTIGDMMQKLSGQLSDARNKENLQPQSSGVQGQVPIS PEPLQRPEMLKEETRSSAAAAADTQDEATGAEEELLPGVDVLL EVFPTCSVEQAQWVLAKARGDLEEAVQMLVEGKEEGPAAWEGP NQDLPRRLRGPQKDELKSFILQKYMMVDSAEDQKIHRPMAPKE APKKLIRYIDNQVVSTKGERFKDVRNPEAEEMKATYINLKPAR KYRFH
570	1309	3	526	FITGKGIVAILRCLQFNETLTELRFHNQRHMLGHHAEMEIARL LKANNTLLKMGYHFELPGPRMVVTNLLTRNQDKQRQKRQEEQK QQQLKEQKKLIAMLENGLGLPPGMWELLGGPKPDSRMQEFFQP PPPRPPNPQNVPFSQRSEMMKKPSQAPKYRTDPDSFRVVKLKR IQ
571	1310	3	1858	GGRAGTQCCWRAGARLRGISPSPALPEAPGLCRVRAGLGAGAL GRSPAGRRRRGPRVSSSPAPHPRRVLCRCLLFLFFSCHDRRGD SQPYQALKYSSKSHPSSGDHRHEKMRDAGDPSPPNKMLRRSDS PENKYSDSTGHSKAKNVHTHRVRERDGGTSYSPQENSHNHSAL HSSNFTFFLIPSN*PQGKTFRIAPYDS\ADDW/SLEHISSSGE KYYYNCRTEVSQWGKTPKSGLERGQRQKEANKMAVNSFPKDRD YRREVMQATATSGFASGKSTSGDKPVSHSCTTPSTSSASGLNP TSAPPTSASA\VPVSP\VPQ\SPIPPLLQDPNLLRQLL\PALE ATLQLNNSNVDI\SIINEVLTGDVTQASLQTIIHKCLTAGPSV FKITSLISQAAQLSTQAQASNQSPMSLTSDASSPR\SYVSPRN KAHLKLNTVPIQTFGFSTPPVSSQPKVSTPVVKQGPVSQSATQ QPVTADKQQGHEPVSPRSLQRSSSQRSPSPGPNHTSNSSNASN ATVVPQNSSARSTCSLTPALAAHFSENLIKHVQGWPADHAEKQ ASRLREEAHNMGTIHMSEICTELKNLRSLVRVCEIQATLREQR ILFLRQQIKELEKLKNQNSFMV
572	1311	2	1165	VAPECRGAYPFRAMMPGTALKAVLLAVLLVGLQTATGRLLSGQ PVCRGGTQRPCYKVIYFHDTSRRLNFEEAKEACRRDGGQLVSI ESEDEQKLIEKFIENLLPSDGDFWIGLRRREEKQSNSTACQDL YAWTDGSISQFRNWYVDEPSCGSEVCVVMYHQPSAPAGIGGPY MFQWNDDRCNMKNNFICKYSDEKPAVPSREAEGEETELTTPVL PEETQEEDAKKTFKESREAALNLAYILIPSIPLLLLLVVTTVV CWVWICRKRKREQPDPSTKKQHTIWPSPHQGNSPDLEVYNVIR KQSEADLAETRPDLKNISFRVCSGEATPDDMSCDYDNMAVNPS ESGFVTLVSVESGFVTNDIYEFSPDQMGRSKESGWVENEIYGY

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573	1312	3	1416	TEWGLSGSCPGCSPLEPGSRGRGAAAWRILRCRRLPEPSPFLT QPNLAQSQPPAPVPVTDPSVTMHPAVFLSLPDLRCSLLLLVTW VFTPVTTEITSLDTENIDEILNNADVALVNFYADWCRFSQMLH PIFEEASDVIKEEFPNENQVVFARVDCDQHSDIAQRYRISKYP TLKLFRNGMMMKREYRGQRSVKALADYIRQQKSDPIQEIRDLA EITTLDRSKRNIIGYFEQKDSDNYRVFERVANILHDDCAFLSA FGDVSKPERYSGDNIIYKPPGHSAPDMVYLGAMTNFDVTYNWI QDKCVPLVREITFENGEELTEEGLPFLILFHMKEDTESLEIFQ NEVARQLISEKGTINFLHADCDKFRHPLLHIQKTPADCPVIAI DSFRHMYVFGDFKDVLIPGKLKQFVFDLHSGKLHREFHHGPDP TDTAPGEQAQDVASSPPESSFQKLAPSEYRYTLLRDRDEL
574	1313	928	142	LTPSVGPVFPGRPTRPLASPFPVPLHRCSAGSQPPGPVPEGLI RIYSMRFCPYSHRTRLVLKAKDIRHEVVNINLRNKPEWYYTKH PFGHIPVLETSQCQLIYESVIACEYLDDAYPGRKLFPYDPYER ARQKMLLELFCKVPHLTKECLVALRCGRECTNLKAALRQEFSN LEEILEYQNTTFFGGTCISMIDYLLWPWFERLDVYGILDCVSH TPALRLWISAMKWDPTVCALLMDKSIFQGFLNLYFQNNPNAFD FGLC
575	1314	884	363	NTATNMTQPNAGTRKYSVPAISVHTSSSSFAYDREFLRTLPGF LIVAEIVLGLLVWTLIAGTEYFRVPAFGWVMFVAVFYWVLTVF FLIIYITMTYTRIPQVPWTTVGLCFNGSAFVLYLSAAVVDASS VSPERDSHNFNSWAASSFFAFLVTICYAGNTYFSFIAWRSRTI Q
576	1315	165	944	GLRDPFRRKRRLKPQVKMSNYVNDMWPGSPQEKDSPSTSRSGG SSRLSSRSRSRSFSRSSRSHSRVSSRFSSRSRRSKSRSRSRRR HQRKYRRYSRSYSRSRSRSRSRRYRERRYGFTRRYYRSPSRYR SRSRSRSRSRGRSYCGRAYAIARGQRYYGFGRTVYPEEHSRWR DRSRTRSRSRTPFRLSEKDRMELLEIAKTNAAKALGTTNIDLP ASLRTVPSAKETSRGIGVSSNGAKPEVSILGLSEQNFQKANCQ I

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577	1316	265	2300	AEGSTMDLTKMGMIQLQNPNHPTGLLCKANQMRLAGTLCDVVI MVDSQEFHAHRTVLACTSKMFEILFHRNSQHYTLDFLSPKTFQ QILEYAYTATLQAKAEDLDDLLYAAEILEIEYLEEQCLKMLET IQASDDNDTEATMADGGAEEKKDRKARYLKNIFISKHSSEESG YASVAGQSLPGPMVDQSPSVSTSFGLSAMSPTKAAVDSLMTIG QSLLQGTLQPPAGPEEPTLAGGGRHPGVAEVKTEMMQVDEVPS QDSPGAAESSISGGMGDKVEERGKEGPGTPTRSSVITSARELH YGREESAEQVPPPAEAGQAPTGRPEHPAPPPEKHLGIYSVLPN HKADAVLSMPSSVTSGLHVQPALAVSMDFSTYGGLLPQGFIQR ELFSKLGELAVGMKSESRTIGEQCSVCGVELPDNEAVEQHRKL HSGMKTYGCELCGKRFLDSLRLRMHLLAHSAGAKAFVCDQCGA QFSKEDALETHRQTHTGTDMAVFCLLCGKRFQAQSALQQHMEV HAGVRSYICSECNRTFPSHTALKRHLRSHTGDHPYECEFCGSC FRDESTLKSHKRIHTGEKPYECNGCGKKFSLKHQLETHYRVHT GEKPFECKLCHQRSRDYSAMIKHLRTHNGASPYQCTICTEYCP SLSSMQKHMKGHKPEEIPPDWRIEKTYLYLCYV
578	1317	686	908	IWEAPTLIFTLAGGRALGHPPMQKGSQGCALPHPLPGASLPAQ PGPADHRGWECRIGGEASVFTHLFCLPHSPT
579	1318	150	1204	ASGSPAPSSSSAMAAACGPGAAGYCLLLGLHLFLLTAGPALGW NDPDRMLLRDVKALTLHYDRYTTSRRLDPIPQLKCVGGTAGCD SYTPKVIQCQNKGWDGYDVQWECKTDLDIAYKFGKTVVSCEGY ESSEDQYVLRGSCGLEYNLDYTELGLQKLKESGKQHGFASFSD YYYKWSSADSCNMSGLITIVVLLGIAFVVYKLFLSDGQYSPPP YSEYPPFSHRYQRFTNSAGPPPPGFKSEFTGPQNTGHGATSGF GSAFTGQQGYENSGPGFWTGLGTGGILGYLFGSNRAATPFSDS WYYPSYPPSYPGTWNRAYSPLHGGSGSYSVCSNSDTKTRTASG YGGTRRR
580	1319	1208	276	GRCGAMAAGLARLLLLLGLSAGGPAPAGAAKMKVVEEPNAFGV NNPFLPQASRLQAKRDPSPVSGPVHLFRLSGKCFSLVESTYKY EFCPFHNVTQHEQTFRWNAYSGILGIWHEWEIANNTFTGMWMR DGDACRSRSRQSKVELACGKSNRLAHVSEPSTCVYALTFETPL VCHPHALLVYPTLPEALQRQWDQVEQDLADELITPQGHEKLLR TLFEDAGYLKTPEENEPTQLEGGPDSLGFETLENCRKAHKELS KEIKRLKGLLTQHGIPYTRPTETSNLEHLGHETPRAKSPEQLR GDPGLRGSL
581	1320	1074	132	NSFWSVLFLVQEETEVARCNAQHRLRQSRDSKPDPSFRSQPID SSISFAGSDIQPLFSFASVDGTQVGEAEEWAGPWAEATLLPGP GNRWPPRAGLSGNWLEEDGDWPSLPEVVGFVSERELFRDALGA GCRILLICEMQLTHQLDLFPECRVTLLLFKDVKNAGDLRRKAM EGTIDGSLINPTVIVDPFQILVAANKAVHLYKLGKMKTRTLST EIIFNLSPNNNISEALKKFGISANDTSILIVYIEEGEKQINQE YLISQVEGHQVSLKNLPEIMNITEVKKIYKLSSQEESIGTLLD AIICRMSTKDVL

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582	1321	5021	7694	QRSWAGPGAGPEAGTRPPARGRRRQPGNVDPRRRAPQLRSQMQ VAMARATTATGNRLWPGLLIMLGSLCHRGSPCGLSTHIEIGHR ALEFLQLHNGRVNYRELLLEHQDAYQAGIVFPDCFYPSICKGG KFHDVSESTHWTPFLNASVHYIRENYPLPWEKDTEKLVAFLFG ITSHMAADVSWHSLGLEQGFLRTMGAIDFHGSYSEAHSAGDFG GDVLSQFEFNFNYLARRWYVPVKDLLGIYEKLYGRKVITENVI VDCSHIQFLEMYGEMLAVSKLYPTYSTKSPFLVEQFQEYFLGG LDDMAFWSTNIYHLTIFMLENGTSDCNLPENPLFIACGGQQNH TQGSKMQKNDFHRNLTTSLTESVDRNINYTERGVFFSVNSWTP DSMSFIYKALERNIRTMFIGGSQLSQKHVSSPLASYFLSFPYA RLGWAMTSADLNQDGHGDLVVGAPGYSRPGHIHIGRVYLIYGN DLGLPPVDLDLDKEAHRILEGFQPSGRFGSALAVLDFNVDGVP DLAVGAPSVGSEQLTYKGAVYVYFGSKQGGMSSSPNITISCQD IYCNLGWTLLAADVNGDSEPDLVIGSPFAPGGGKQKGIVAAFY SGPSLSDKEKLNVEAANWTVRGEEDFSWFGYSLHGVTVDNRTL LLVGSPTWKNASRLGHLLHIRDEKKSLGRVYGYFPPNGQSWFT ISGDKAMGKLGTSLSSGHVLMNGTLKQVLLVGAPTYDDVSKVA FLTVTLHQGGATRMYALTSDAQPLLLSTFSGDRRFSRFGGVLH LSDLDDDGLDEIIMAAPLRIADVTSGLIGGEDGRVYVYNGKET TLGDMTGKCKSWITPCPEEKAQYVLISPEASSRFGSSLITVRS KAKNQVVIAAGRSSLGARLSGALHVYSLGSD
583	1322	1	357	SLRNSARGLKMAASAARGAAALRRSINQPVAFVRRIPWTAASS QLKEHFAQFGHVRRCILPFDKETGFHRGLGWVQFSSEEGLRNA LQQENHIIDGVKVQVHTRRPKLPQTSDDEKKDF
584	1323	1205	433	GSSNIHSASTHGFCHWFSSPSTLKRQKQAIRFQKIRRQMEAPG APPRTLTWEAMEQIRYLHEEFPESWSVPRLAEGFDVSTDVIRR VLKSKFLPTLEQKLKQDQKVLKKAGLAHSLQHLRGSGNTSKLL PAGHSVSGSLLMPGHEASSKDPNHSTALKVIESDTHRTNTPRR RKGRNKEIQDLEESFVPVAAPLGHPRELQKYSSDSESPRGTGS GALPSGQKLEELKAEEPDNFSSKVVQRGREFFDSNGNFLYRI
585	1324	134	954	ETRVKTSLELLRTQLEPTGTVGNTIMTSQPVPNETIIVLPSNV INFSQAEKPEPTNQGQDSLKKHLHAEIKVIGTIQILCGMMVLS LGIILASASFSPNFTQVTSTLLNSAYPFIGPFFFIISGSLSIA TEKRLTKLLVHSSLVGSILSALSALVGFIILSVKQATLNPASL QCELDKNNIPTRSYVSYFYHDSLYTTDCYTAKASLAGTLSLML ICTLLEFCLAVLTAVLRWKQAYSDFPGSVLFLPHSYIGNSGMS SKMTHDCGYEELLTS

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586	1325	106	1537	EMVGAMWKVIVSLVLLMPGPCDGLFRSLYRSVSMPPKGDSGQP LFLTPYIEAGKIQKGRELSLVGPFPGLNMKSYAGFLTVNKTYN SNLFFWFFPAQIQPEDAPVVLWLQGGPGGSSMFGLFVEHGPYV VTSNMTLRDRDFPWTTTLSMLYIDNPVGTGFSFTDDTHGYAVN EDDVARDLYSALIQFFQIFPEYKNNDFYVTGESYAGKYVPAIA HLIHSLNPVREVKINLNGIAIGDGYSDPESIIGGYAEFLYQIG LLDEKQKKYFQKQCHECIEHIRKQNWFEAFEILDKLLDGDLTS DPSYFQNVTGCSNYYNFLRCTEPEDQLYYVKFLSLPEVRQAIH VGNQTFNDGTIVEKYLREDTVQSVKPWLTEIMNNYKVLIYNGQ LDIIVAAALTERSLMGMDWKGSQEYKKAEKKVWKIFKSDSEVA GYIRQAGDFHQVIIRGGGHILPYDQPLRAFDMINRFIYGKGWD PYVG
587	1326	883	541	RDERAKVPFRSTEG\GRRRRRRMEAVVFVFSLLDCCALIFLSV YFIITLSDLECDYINARSCCSKLNKWVIPELIGHTIVTVLLLM SLHWFIFLLNLPVATWNIYRYIMVPSGNMGVFDPTEIHNRGQL KSHMKEAMIKLGFHLLCFFMYLYSMILALIND
588	1327	1126	732	QSPGHGAPCQLSSSHSRSNRLLSPMARATLSAAPSNPRLLRVA LLLLLLVAASRRAAGAPLATELRCQCLQTLQGIHLKNIQSVKV KSPGPHCAQTEVIATLKNGQKACLNPASPMVKKIIEKMLKNGK SN
589	1328	197	330	HPLSLVFLALNTGKEKSHPGGGGERPGLAGQGEPDHPAGARDG R
590	1329	1	1575	CTPVARSMATTATCTRFTDDYQLFEELGKGAFSVVRRCVKKTS TQEYAAKIINTKKLSARDHQKLEREARICRLLKHPNIVRLHDS ISEEGFHYLVFDLVTGGELFEDIVAREYYSEADASHCIHQILE SVNHIHQHDIVHRDLKPENLLLASKCKGAAVKLADFGLAIEVQ GEQQAWFGFAGTPGYLSPEVLRKDPYGKPVDIWACGVILYILL VGYPPFWDEDQHKLYQQIKAGAYDFPSPEWDTVTPEAKNLINQ MLTINPAKRITADQALKHPWVCQRSTVASMMHRQETVECLRKF NARRKLKGAILTTMLVSRNFSAAKSLLNKKSDGGVKPQSNNKN SLVSPAQEPAPLQTAMEPQTTVVHNATDGIKGSTESCNTTTED EDLKVRKQEIIKITEQLIEAINNGDFEAYTKICDPGLTSFEPE ALGNLVEGMDFHKFYFENLLSKNSKPIHTTILNPHVHVIGEDA ACIAYIRLTQYIDGQGRPRTSQSEETRVWHRRDGKWLNVHYHC SGAPAAPLQ
591	1330	17	636	NRRTVKMLLELSEEHKEHLAFLPQVDSAVVAEFGRIAVEFLRR GANPKIYEGAARKLNVSSDTVQHGVEGLTYLLTESSKLMISEL DFQDSVFVLGFSEELNKLLLQLYLDNRKEIRTILSEL\APSLP SYHNLEWRLDVQLASRSLRQQIKPAVTIKLHLNQNGDHNTKVL QTDPATLLHLVQQLEQALEEMKTNHCRRVVRNIK
592	1331	1	237	GTSIYLAHRVA\RAWELAQFIHHTSKKADVVLACGDSIVHPED LICCPLTGRSCLCDVHLLSSLLARLGRGYAVSLTNL

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593	1332	2506	1684	RGCGSCGYKPSAGPAWRPRPPPAVSPLRHPEPAKVLSFSSCPL PALGRTGPSRAARAQSLTMASLFKKKTVDDVIKEQNRELRGTQ RAIIRDRAALEKQEKQLELEIKKMAKIGNKEACKVLAKQLVHL RKQKTRTFAVSSKVTSMSTQTKVMNSQMKMAGAMSTTAKTMQA VNKKMDPQKTLQTMQNFQKENMKMEMTEEMINDTLDDIFDGSD DEEESQDIVNQVLDEIGIEISGKMAKAPSAARSLPSASTSKAT ISDEEIERQLKALGVD
594	1333	905	432	STDGNGAERLFAELRKMNARGLGSELKDSIPVTELSASGPFES HDLLRKGFSCVKNELLPSHPLELSEKNFQLNQDKMNFSTLRNI QGLFAPLKLQMEFKAVQQVQRLPFLSSSNLSLDVLRGNDETIG FEDILNDPSQSEVMGEPHLMVEYKLGLL
595	1334	111	117	RNMKLHYVAVLTLAILMFLTWLPESLSCNKALCASDVSKCLIQ ELCQCRPGEGNCSCCKECMLCLGALWDECCDCVGMCNPRNYSD TPPTSKSTVEELHEPIPSLFRALTEGDTQLNWNIVSFPVAEEL SHHENLVSFLETVNQPHHQNVSVPSNNVHAPYSSDK/E*LPTV DFFHSAPSCGLSM*SIIFFEET
596	1335	817	278	VGGVPTWLEGCGSGNPSPRSGGGPGARLTLPALQMTVHNLYLF DRNGVCLHYSEWHRKKQAGIPKEEEYKLMYGMLFSIRSFVSKM SPLDMKDGFLAFQTSRYKLHYYETPTGIKVVMNTDLGVGPIRD VLHHIYSALYVELVVKNPLCPLGQTVQSELFRSRLDSYVRSLP FFSARAG
597	1336	171	881	PGLSQEPSGSMETVVIVAIGVLATIFLASFAALVLVCRQRYCR PRDLLQRYDSKPIVDLIGAMETQSEPSELELDDVVITNPHIEA ILENEDWIEDASGLMSHCIAILKICHTLTEKLVAMTMGSGAKM KTSASVSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTAL LLSVSHLVLVTRNACHLTGGLDWIDQSLSAAEEHLEVLREAAL ASEPDKGLPGPEGFLQEQSAI
598	1337	1078	594	VGMELPAVNLKVILLGHWLLTTWGCIVFSGSYAWANFTILALG VWAVAQRDSIDAISMFLGGLLATIFLDIVHISIFYPRVSLTDT GRFGVGMAILSLLLKPLSCCFVYHMYRERGGELLVHTGFLGSS QDRSAYQTIDSAEAPADPFAVPEGRSQDARGY
599	1338	717	116	PASRPLLGPDTGSVANIFKGLVILPEMSLVIRNLQRVIPIRRA PLRSKIEIVRRILGVQKFDLGIICVDNKNIQHINRIYRDRNVP TDVLSFPFHEHLKAGEFPQPDFPDDYNLGDIFLGVEYIFHQCK ENEDYNDVLTVTATHGLCHLLGFTHGTEAEWQQMFQKEKAVLD ELGRRTGTRLQPLTPGPLPEGAEGRVPF
600	1339	1	804	LRNALDVLHREVPRVLVNLVDFLNPTIMRQVFLGNPDKCPVQQ A/MLEPLGSKTETLDLRAEMPITCPTQNEPFLRTPRNSNYTYP IKPAIENWGSDFLCTEWKASNSVPTSVHQLRPADIKVVAALGD SLTTAVGARPNNSSDLPTSWRGLSWSIGGDGNLETHTTLPNIL KKFNPYLLGFSTSTWEGTAGLNVAAEGARARDMPAQAWDLVER MKNSPDINLEKDWKLVTLFIGGNDLCHYCENPEAHLATEYVQH IQQALDILSE

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601	1340	1	860	VVEFLWSRRPSGSSDPRPRRPASKCQMMEERANLMHMMKLSIK VLLQSALSLGRSLDADHAPLQQFFVVMEHCLKHGLKVKKSFIG QNKSFFGPLELVEKLCPEASDIATSVRNLPELKTAVGRGRAWL YLALMQKKLADYLKVLIDNKHLLSEFYEPEALMMEEEGMVIVG LLVGLNVLDANL\CLKGEDLDSQVGVIDFSLYLKDVQDLDGGK EHERITDVLDQKNYVEELNRHLSCTVGDLQTKIDGLEKTNSKL QERVSAATDRICSLQEEQQQLREQNELIR
602	1341	60	762	KPEGARRVQFVMGLFGKTQEKPPKELVNEWSLKIRKEMRVVDR QIRDIQREEEKVKRSVKDAAKKGQKDVCIVLAKEMIRSRKAVS KLYASKAHMNSVLMGMKNQLAVLRVAGSLQKSTEVMKAMQSLV KIPEIQATMRELSKEMMKAGIIEEMLEDTFESMDDQEEMEEEA EMEIDRILFEITAGALGKAPSKVTDALPEPEPPGAMAASEDEE EEEEALEAMQSRLATLRS
603	1342	3	456	RWNSIMELALLCGLVVMAGVIPIQGGILNLNKMVKQVTGKMPI LSYWPYGCHCGLGGRGQPKDATDWCCQTHDCCYDHLKTQGCGI YKDYYRYNFSQGNIHCSDKGSWCEQQLCACDKEVAFCLKRNLD TYQKRLRFYWRPHCRGQTPGC
604	1343	249	632	KTVAEEASVGNPEGAFMKMLQARKQHMSTELTIESEAPSDSSG INLSGFGSEQLDTNDESDVSSALSYILPYLSLRNLGAESILLP FTEQLFSNVQDGDRLLSILKNNRKSPSQSSLLGNKFKNKIF
605	1344	2	382	LPLTLLLAAPFAHLLLPPGHDQSPCWHPGPALSPGTLGPLSWA MANSGLQLLGYFLALGGWVGIIASTALPQWKQSSYAGDASIQL RSKVFVLESEWGGDSLGLPRDCGWSCLLHSAVRSEKGFWS
606	1345	2	987	DPRVRPPLLQPPPPLLPRLVILKMAPLDLDKYVEIARLCKYLP ENDLKRLCDYVCDLLLEESNVQPVSTPVTVCGDIHGQFYDLCE LFRTGGQVPDTNYIFMGDFVDRGYYSLETFTYLLALKAKWPDR ITLLRGNHESRQITQVYGFYDECQTKYGNANAWRYCTKVFDML TVAALIDEQILCVHGGLSPDIKTLDQIRTIERNQEIPHKGAFC DLVWSDPEDVDTWAISPRGAGWLFGAKVTNEFVHINNLKLICR AHQLVHEGYKFMFDEKLVTVWSAPNYCYRCGNIASIMVFKDVN TREPKLFRAVPDSERVIPPRTTTPYFL
607	1346	10	768	SFAGAAARPSTPPASGRGAAPGRPGPSPMDLRAGDSWGMLACL CTVLWHLPAVPALNRTGDPGPGPSIQKTYDLTRYLEHQLRSLA GTYLNYLGPPFNEPDFNPPRLGAETLPRATVDLEVWRSLNDKL RLTQNYEAYSHLLCYLRGLNRQAATAELRRSLAHFCTSLQGLL GSIAGVMAALGYPLPQPLPGTEPTWTPGPAHSDFLQKMDDFWL LKELQTWLWRSAKDFNRLKKKMQPPAAAVTLHLGAHGF
608	1347	114	700	IKISLKKRSMSGISGCPFFLWGLLALLGLALVISLIFNISHYV EKQRQDKMYSYSSDHTRVDEYYIEDTPIYGNLDDMISEPMDEN CYEQMKARPEKSVNKMQEATPSAQATNETQMCYASLDHSVKGK RRKPRKQNTHFSDKDGDEQLHAIDASVSKTTLVDSFSPESQAV EENIHDDPIRLFGLIRAKREPIN

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609	1348	2	807	VEFHPQRARAGARAPSMGVLLTQRTLLSLVLALLFPSMASMAA IGSCSKEYRVLLGQLQKQTDLMQDTSRLLDPYIRIQGLDVPKL REHCRERPGAFPSEETLRGLGRRCFLQTLNATLGCVLHRLADL EQRLPKAQDLERSGLNIEDLEKLQMARPNILGLRNNIYCMAQL LDNSDTAEPTKAGRGASQPPTPTPASDAFQRKLEGCRFLHGYH RFMHSVGRVFSKWGESPNRSRRHSPHQALRKGVRRTRPSRKGK RLMTRGQLPR
610	1349	2	418	DFPGRRFRLVWLLVLRLPWRVPGQLDPTTGRRFSEHKLCADDE CSMLMYRGEALEDFTGPDCRFVNFKKGDPVYVYYKLARGWPEV WAGSVGRTFGYFPKDLIQVVHEYTKEELQVPTNETDFVCFDGG RDDFHNYNV
611	1350	823	115	SPLGKEGQEEVRVKIKDLNEHIVCCLCAGYFVDATTITECLHT FCKSCIVKYLQTSKYCPMCNIKIHETQPLLNLKLDRVMQDIVY KLVPGLQDSEEKRIREFYQSRGLDRVTQPTGEEPALSNLGLPF SSFDHSKAHYYRYDEQLNLCLERLSSGKDKNKSVLQNKYVRCS VRAEVRHLRRVLCHRLMLNPQHVQLLFDNEVLPDHMTMKQIWL SRWFGKPSPLLLQYSVKEKRR
612	1351	9	545	LWWYSAHAAVDAMMDVFGVGFPSKVPWKKMSAEELENQYCPSR WVVRLGAEEALRTYSQIGIEATTRARATRKSLLHVPYGDGEGE KVDIYFPDESSEATTRARATRKSLLHVPYGDGEGEKVDIYFPD ESSEALPFFLFFHGGYWQSGRHPGPHGRPGDPQRCVCPEAVSK QQAFSW
613	1352	49	902	GVRMASRGRRPEHGGPPELFYDETEARKYVRNSRMIDIQTRMA GRALELLYLPENKPCYLLDIGCGTGLSGSYLSDEGHYWVGLDI SPAMLDEAVDREIEGDLLLGDMGQGIPFKPGTFDGCISISAVQ WLCNANKKSENPAKRLYCFFASLFSVLVRGSRAVLQLYPENSE QLELITTQATKAGFSGGMVVDYPNSAKAKKFYLCLFSGPSTFI PEGLSENQDEVEPRESVFTNERFPLRMSRRGMVRKSRAWVLEK KERHRRQGREVRPDTQYTGRKRKPRF
614	1353	1960	871	TLICRMAGCGEIDHSINMLPTNRKANESCSNTAPSLTVPECAI CLQTCVHPVSLPCKHVFCYLCVKGASWLGKRCALCRQEIPEDF LDKPTLLSPEELKAASRGNGEYAWYYEGRNGWWQYDERTSREL EDAFSKGKKNTEMLIAGFLYVADLENMVQYRRNEHGRRRKIKR DIIDIPKKGVAGLRLDCDANTVNLARESSADGADSVSAQSGAS VQPLVSSVRPLTSVDGQLTSPATPSPDASTSLEDSFAHLQLSG DNTAERSHRGEGEEDHESPSSGRVPAPDTSIEETESDASSDSE DVSAVVAQHSLTQQRLLVSNANQTVPDRSDRSGTDRSVAGGGT VSVSVRSRRPDGQCTVTEV

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615	1354	5653	4549	GATPLGSVGGRTGKMDAATLTYDTLRFAEFEDFPETSEPVWIL GRKYSIFTEKDEILSDVASRLWFTYRKNFPAIGGTGPTSDTGW GCMLRCGQMIFAQALVCRHLGRDWRWTQRKRQPDSYFSVLNAF IDRKDSYYSIHQIAQMGVGEGKSIGQWYGPNTVAQVLKKLAVF DTWSSLAVHIAMDNTVVMEEIRRLCRTSVPCAGATAFPADSDR HCNGFPAGAEVTNRPSPWRPLVLLIPLRLGLTDINEAYVETLK HCFMMPQSLGVIGGKPNSAHYFIGYVGEELIYLDPHTTQPAVE PTDGCFIPDESFHCQHPPCRMSIAELDPSIAVVRGGHLSTQAF GAECCLGMTRKTFGFLRFFFSMLG
616	1355	416	65	PTTSNRAITLTAWPKIPFLGICEAKNPRSENMRLATILEVACH HLGSGPPPSWELWEQGPPGNSSRYIEFLNKHTYIKGTLRVYTK KFCMLVIKSFESKSCVCVYDFDSKSSVNVTV
617	1356	2	382	PRVRFRLLHVTSIRSAWILCGIIWILIMASSIMLLDSGSEQNG SVTSCLELNLYKIAKLQTVNYIALVVGCLLPFFTLSICYLLII RVLLKVEVPESGLRVSHRKALTTIIITLIIFFLCFLPYHT
618	1357	3	672	GRHWLGSAQLTDGGSARKPKMAVPAALILRESPSMKKAVSLIN AIDTGRFPRLLTRILQKLHLKAESSFSEEEEEKLQAAFSLEKQ DLHLVLETISFILEQAVYHNVKPAALQQQLENIHLRQDKAEAF VNTWSSMGQETVEKFRQRILAPCKLETVGWQLNLQMAHSAQAK LKSPQAVLQLGVNNEDSKSLEKVLVEFSHKELFDFYNKLETIQ AQLDSLT
619	1358	557	208	EASSAKTKRKEEKGPKAKMKLMVLVFTIGLTLLLGVQAMPANR LSCYRKILKDHNCHNLPEGVADLTQIDVNVQDHFWDGKGCEMI CYCNFSELLCCPKDVFFGPKISFVIPCNNQ
620	1359	335	1735	KMAEAVFHAPKRKRRVYETYESPLPIPFGQDHGPLKEFKIFRA EMINNNVIVRNAEDIEQLYGKGYFGKGILSRSRPSFTISDPKL VAKWKDMKTNMPIITSKRYQHSVEWAAELMRRQGQDESTVRRI LKDYTKPLEHPPVKRNEEAQVHDKLNSGMVSNMEGTAGGERPS VVNGDSGKSGGVGDPREPLGCLQEGSGCHPTTESFEKSVREDA SPLPHVCCCKQDALILQRGLHHEDGSQHIGLLHPGDRGPDHEY VLVEEAECAMSEREAAPNEELVQRNRLICRRNPYRIFEYLQLS LEEAFFLVYALGCLSIYYEKEPLTIVKLWKAFTVVQPTFRTTY MAYHYFRSKGWVPKVGLKYGTDLLLYRKGPPFYHASYSVIIEL VDDHFEGSLRRPLSWKSLAALSRVSVNVSKELMLCYLIKPSTM TDKEMESPECMKRIKVQEVILSRWVSSRERSDQDDL

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621	1360	5693	4435	RDIWTMNLQRYWGEIPISSSQTNRSSFDLLPREFRLVEVHDPP LHQPSANKPKPPTMLDIPSEPCSLTIHTIQLIQHNRRLRNLIA TAQAQNQQQTEGVKTEESEPLPSCPGSPPLPDDLLPLDCKNPN APFQIRHSDPESDFYRGKGEPVTELSWHSCRQLLYQAVATILA HAGFDCANESVLETLTDVAHEYCLKFTKLLRFAVDREARLGQT PFPDVMEQVFHEVGIGSVLSLQKFWQHRIKDYHSYMLQISKQL SEEYERIVNPEKATEDAKPVKIKEEPVSDITFPVSEELEADLA SGDQSLPMGVLGAQSERFPSNLEVEASPQASSAEVNASPLWNL AHVKMEPQESEEGNVSGHGVLGSDVFEEPMSGMSEAGIPQSPD DSDSSYGSHSTDSLMGSSPVFNQRCKKRMRKI
622	1361	15	678	REQILFIEIRDTAKGGETEQPPSLSPLHGGRMPEMGEGIQSLA RETQSHRGRRQGWDATWVTRCRESLNRGGAGAGKRAGALAHHV FLALIEPNLAEREASEEEVKACSDETVVADLLVKVVYVLGAIL KIFLREGNVLNQHSGMDIEKYSEHYQHDHSPGAEDDAAGGQLR PTAQERRHKEGSRGSPRCKRARKAVGESPGCPRPRVRPRVRPR VRPRV
623	1362	1080	835	GTRGCCREGTAYAKAYQFMASHLSLGKPVSTGSIPRFNKALFN KQAKCKPNHYSFIGLSMLSPENFSIGCKYSVWFSETKGF
624	1363	872	441	GAQGVRVGIGEVGRVQAPRVSLLHSQGVPRGGTGEAVKEEGRG SSLHPPLPPQGLGEYAACQSHAFMKGVFTFVTGTGMAFGLQMF IQRKFPYPLQWSLLVAVVAGSVVSYGVTRVESEKCNNLWLFLE TGQLPKDRSTDQRS
625	1364	1	585	GTSELLCIQRWNWGPAFPPRPGLALAPTLQLLVEMGSAKSVPV TPARPPPHNKHLARVADPRSPSAGILRTPIQVESSPQPGLPAG EQLEGLKHAQDSDPRSPLGKN*GHGWQVGQGSDLGSPQPLPPS ASHL/YSSRASRCSQPPCLSLPWFGVRSSPANTYHVPVTSLCP SPALHYTALQAGIISTSQARAPR
626	1365	36	381	PLLLPRFIDIPCLLCYLTQVTPDDMYAKAFLIKPNTAITGTDR RKL\RADETTDFP\TLGTDQIYELLPGKDELNIVKSNAHKRDA *TAYVSGENHILSEP*KNLYPAVNTLSSYP
627	1366	763	1003	SRQPPPLLTMVFLLEFLFLVFFPGCVNQLLLSYPWQGQGTSLW SSLSFHWLLPQEDSSRLSIFPLRAGSPPQPAQAPQRI
628	1367	296	1199	KSREQSSLFAADAERSWGGKSCCLLRWRFVGKASHFPRLLPLP GEERPETKERAWKMEQTWTRDYFAEDDGEMVPRTSHTA/ASVS LTAFLSDTKDRGPPVQSQIWRSGEKVPFVQTYSLRAFEKPPQV QTQALRDFEKHLNDLKKENFSLKLLIYFLEERMQQKYEASRED IYKRNTELKVEVESLKRELQDKKQHLDKTWADVENLNSQNEAE LRRQFEERQQEMEHVYELLENKMQLLQEESRLAKNEAARMAAL VEAEKECNLELSEKLKGVTKNWEDVPGDQVKPDQYTEALAQRD K

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629	1368	191	1116	TRRRGTTWRSPRPRRASTSRPSTRPRGVASWPWETAGTATTGP GPSARTRRRAARRRRSRPRRRAHGGLSQPAGWQSLLSFTILFL AWLAGFSSRLFAVIRFESIIHEFDPWFNYRSTHHLASHGFYEF LNWFDERAWYPLGRIVGGTVYPGLMITAGLIHWILNTLNITVH IRDVCVFLAPTFSGLTSISTFLLTRELWNQGAGLLAACFIAIV PGYISRSVAGSFDNEGIAIFALQFTYYLWVKSVKTGSVFWTMC CCLSYFYMVSAWGGYVFIINLIPLHAFVLVLM/Q/RYSKRVYI *YSTFYIVG
630	1369	852	214	RRLIVVLSDAFLSRAWCSHSF/RVGPARGWVGPSVAPTPLTVP PRREGLCRLLELTRRPIFITFEGQRRDPAHPALRLLRQHRHLV TLLLWRPGSVTPSSDFWKEVQLALPRKVRYRPVEGDPQTQLQD DKDPMLILRGRVPEGRALDSEVDPDPEGDLGVRGPVFGEPSAP PHTSGVSLGESRSSEVDVSDLGSRNYSARTDFYCLVSKDDM
631	1370	246	1091	LSHEGWRRGREGERINSSVASLAPLCILPDLPSNMHLARLVGS CSLLLLLGALSGWAASDDPIEKVIEGINRGLSNAEREVGKALD GINSGITHAGREVEKVFNGLSNMGSHTGKELDKGVQGLNHGMD KVAHEINHGIGQAGKEAEKLGHGVNNAAGQAGKEADKAVQGFH TGVHQAGKEAEKLGQGVNHAADQAGKEVEKLGQGAHHAAGQAG KELQNAHNGVNQASKEANQLLNGNHQSGSSSHQGGATTTPLAS GASVNTPFINLPALWRSVANIMP
632	1371	3150	2792	SASGGLGMTVEGPEGSEREHRPPEKPPRPPRPLHLSDRSFRRK KDSVESHPTWVDDTRIDADAIVEKIVQSQDFTDGSNTEDSNLR LFVSRDGSATLSGIQLATRVSSGVYEPVVIESH
633	1372	667	993	ERSGWPQPEGTVTAQGPLFWERLSGAVTVSSGYKADMWPSFPQ \VRVGSFLFGILFFSFGSSSLPPGLPPPASLLCCAVQWGARAL FLPCLKERALGMEMRNNTLSFRQ
634	1373	636	2	SSSNLRLSFLINENILGKCFRSGPSCAGPRISPLAAQYECPRP SLLIMASVPKTNKIEPRSYSIIPSCGI\RRLGPALNTLIF\QS KRFGPRG\HSAKSIEGAPRGKGRGRAVARLAADRPPAPKIQLR AF*LQQL*YTLLELELPRLLAPDLPSNGSSLKDLKWTHSNYRA SKESCIVIF\VTTSPGREWVICALAAFLGCGS\LSQAPSPES
635	1374	61	519	LRIINTYFCFKFLIVNYIHGTTKARKPHVLGESLISAMSRQEP KMFVLLYVTSFAICASGQPRGNQLKGENYSPRYICSIPGLPGP PGPPGANGSPGPHGRIGLPGRDGRDGRKGEKGEKGTAGLRGKT GPLGLAGEKGDQGETGKKGPIGPE
636	1375	129	579	FASAMLGSRVDRPKLSVAPSVVLEEDQVLVSPAVDLEAGCRLR DFTEKIMNVKGKVILSMLVVSTVIIVFWEFINSTEGSFLWIYH SKNPEVDDSSAQKGWWFLSWFNNGIHNYQQGEEDIDKEKGREE TKGRKMTQQSFGYGTGLIQT

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637	1376	127	1376	GSHRFSLASPLDPEVGPYCDTPTMRTLFNLLWLALACSPVHTT LSKSDAKKAASKTLLEKSQFSDKPVQDRGLVVTDLKAESVVLE HRSYCSAKARDRHFAGDVLGYVTPWNSHGYDVTKVFGSKFTQI SPVWLQLKRRGREMFEVTGLHDVDQGWMRAVRKHAKGLHIVPR LLFEDWTYDDFRNVLDSEDEIEELSKTVVQVAKNQHFDGFVVE VWNQLLSQKRVGLIHMLTHLAEALHQARLLALLVIPPAITPGT DQLGMFTHKEFEQLAPVLDGFSLMTYDYSTAHQPGPNAPLSWV RACVQVLDPKSKWRSKILLGLNFYGMDYATSKDAREPVVGARY IQTLKDHRPRMVWDSQVSEHFFEYKKSRSGRHVVFYPTLKSLQ VRLELARELGVGVSIWELGQGLDYFYDLL
638	1377	998	48	GREGTGWGPAMSEVTRSLLQRWGASFRRGADFDSWGQLVEAID EYQILARHLQKEAQAQHNNSEFTEEQKKTIGKIATCLELRSAA LQSTQSQEEFKLEDLKKLEPILKNILTYNKEFPFDVQPVPLRR ILAPGEEENLEFEEDEEEGGAGAGSPDSFPARVPGTLLPRLPS EPGMTLLTIRIEKIGLKDAGQCINPYITVSVKDLNGIDLTPVQ DTPVASRKEDTYVHFNVDIELQKHVEKLTKGAAIFFEFKHYKP KKRFTSTKCFAFMEMDEIKLGPIVIELYKKPTDFKRKQLQLLT KKPLYLHLHQTLHKE
639	1378	1298	1569	GSITSEPSLDSLQPLPPGFKRFSCLSLPSSWDYRRPPPGLAYF CIFSRDEVSPCWPGCSPSPDLMIRLPRPPSVGITGVSHRAWPT IDNF
640	1379	196	1197	KMPVPWFLLSLALGRSPVVLSLERLVGPQDATHCSPGLSCRLW DSDILCLPGDIVPAPGPVLAPTHLQTELVLRCQKETDCDLCLR VAVHLAVHGHWEEPEDEEKFGGAADSGVEEPRNASLQAQVVLS FQAYPTARCVLLEVQVPAALVQFGQSVGSVVYDCFEAALGSEV RIWSYTQPRYEKELNHTQQLPDCRGLEVWNSIPSCWALPWLNV SADGDNVHLVLNVSEEQHFGLSLYWNQVQGPPKPRWHKNLVRP PPSQVHSHCRP\CLCK\DAVPYQRGSLKRTHPKQGKIGGGTSA FLVSLTLASSSSSLSSPTSFLYLFHRLDRRSLP
641	1380	756	1110	LRLWNRNQMMHNIIVKELIVTFFLGITVVQMLISVTGLKGVEA QNGSESEVFVGKYETLVFYWPSLLCLAFLLGRFLHMFVKALRV HLGWELQVEEKSVLEVHQGEHVKQLLRIPRP
642	1381	631	1278	KVNRKLRKKGKISHDKRKKSRSKAIGSDTSDIVHIWCPEGMKT SDIKELNIVLPEFEKTHLEHQQRIESKVCKAAIATFYVNVKEQ FIKMLKESQMLTNLKRKNAKMISDIEKKRQRMIEVQDELLRLE PQLKQLQTKYDELKERKSSLRNAAYFLSNLKQLYQDYSDVQAQ EPNVKETYDSSSLPALLFKARTLLGAESHLRNINHQLEKLLDQ G
643	1382	1167	755	VWVAMEEPPVREEE*EEGEEDEERDEVGPEGALGKSPFQLTAE DVYDISYLLGRELMALGSDPRVTQLQFKVVRVLEMLEALVNEG SLALEELKMERDHLRKEVEGLRRQSPPASGEWPDSTKRRPRRK KRKRCCGY

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644	1383	1	271	PRNDHRLTQSRRDSSSKTRAFLVPRFLPAHAGVTSEERTAMKR EGGAAHLCSDSLPESQQQDGNHAPNFSSHGSCRRRQRRRHDKA LHAR
645	1384	1	499	THASEKSRATMSSWSRQRPKSPGGIQPHVSRTLFLLLLLAASA WGVTLSPKDCQVFRSDHGSSISCQPPAEIPGYLPADTVHLAVE FFNLTHLPANLLQGASKLQELHLSSNGLESLSPEFLRPVPQLR VLDLTRNALTGLPPGLFQASATLDTLVLKENQLEVLE
646	1385	178	675	ERPRIMDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLL WPINKQLFRKINCRLSYCISSQLVMLLEWWSGTECTIFTDPRA YLKYGKENAIVVLNHKF\EI\DFLCGWSLSERFGLLGVSQKCI PPCLTHFFGSAPPLVFLLLVIQNLQKNQQSFYLMKWS
647	1386	630	1499	MIVFGWAVFLASRSLGQGLLLTLEEHIAHFLGTGGAATTMGNS CICRDDSGTDDSVDTQQQQAENSAVPTADTRSQPRDPVRPPRR GRGPHEPRRKKQNVDGLVLDTLAVIRTLVDNDQEPPYSMITLH EMAETDEGWLDVVQSLIRVIPLEDPLGPAVITLLLDECPLPTK DALQKLTEILNLNGEVACQDSSHPAKHRNTSAVLGCLAEKLAG PASIGLLSPGILEYLLQCLLQSHPTVMLFALIALEKFAQTSEN KLTISESSISDRL\VTLESW\ANDPDYLKRQVG
648	1387	1	962	RFGTRGLAKSKGVVLMALCALTRALRSLNLAPPTVAAPAPSLF PAAQMMNNGLLQQPSALMLLPCRPVLTSVALNANFVSWKSRTK YTITPVKMRKSGGRDHTGRIRVHGIGGGHKQRYRMIDFLRFRP EETKSGPFEEKVIQVRYDPCRSADIALVAGGSRKRWIIATENM QAGDTILNSNHIGRMAVAAREGDAHPLGALPVGTLINNVESEP GRGAQYIRAAGTCGVLLRKVNGTAIIQLPSKRQMQVLETCVAT VGRVSNVDHNKRVIGKAGRNRWLGKRPNSGRWHRKGGWAGRKI RPLPPMKSYVKLPSASAQS
649	1388	291	714	PVQGARCWLDARRNVRVFSGVCCGCGIHGYWAEPCGGCGAMEG LRSSVELDPELTPGKLDEEMVGLPPHDASPQVTFHSLDGKTVV CPHFMGLLLGLLLLLTLSVRNQLCVRGERQLAETLHSQVKEKS QLIGKKTDCRD
650	1389	874	2220	GARGRPLAETWPFLTAPVLPGQLQITEPTMAEKGDCIASVYGY DLGGRFVDFQPLGFGVNGLVLSAVDSRACRKVAVKKIALSDAR SMKHALREIKIIRRLDHDNIVKVYEVLGPKGTDLQGELFKFSV AYIVQEYMETDLARLLEQGTLAEEHAKLFMYQLLRGLKYIHSA NVLHRDLKPANIFISTEDLVLKIGDFGLARIVDQHYS\HKGYL SEGLVTKWYRSPRLLLSPNNYTKAIDMWAAGCILAEMLTGRML FAGAHELEQMQLILETIPVIREEDKDELLRVMPSFVSSTWEVK RPLRKLLPEVNSEAIDFLEKILTFNPMDRLTAEMGLQHPYMSP YSCPEDEPTSQHPFRIEDEIDDIVLMAANQSQLSNWDTCSSRY PVSLSSDLEWRPDRCQDASEVQRDPRAGSAPLAENVQVDPRKD SHSSSASCQAGRNGVSRYQ

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651	1390	1	2451	MRTLGTCLATLAGLLLTAAGETFSGGCLFDEPYSTCGYSQSEG DDFNWEQVNTLTKPTSDPWMPSGSFMLVNASGRPEGQRAHLLL PQLKENDTHCIDFHYFVSSKSNSPPGLLNVYVKVNNGPLGNPI WNISGDPTRTWNRAELAISTFWPNFYQVIFEVITSGHQGYLAI DEVKVLGHPCTRTPHFLRIQNVEVNAGQFATFQCSAIGRTVAG DRLWLQGIDVRDAPLKEIKVTSSRRFIASFNVVNTTKRDAGKY RCMI\RTEGGVGISNYAEL\VVKEPPVPIAPPQLASVGATYLW IQLNANSINGDGPIVAREVEYCTASGSWNDRQPVDSTSYKIGH LDPDTEYEISVLLTRPGEGGTGSPGPALRTRTKCADPMRGPRK LEVVEVKSRQITIRWEPFGYNVTRCHSYNLTVHYCYQVGGQEQ VREEVSWDTENSHPQHTITNLSPYTNVSVKLILMNPEGRKESQ ELIVQTDEDLPGAVPTESIQGSTFEEKIFLQWREPTQTYGVIT LYEITYKAVSSFDPEIDLSNQSGRVSKLGNETHFLFFGLYPGT TYSFTIRASTAKGFGPPATNQFTTKISAPSMPAYELETPLNQT DNTVTVMLKPAHSRGAPVSVYQIVVEEERPRRTKKTTEILKCY PVPIHFQNASLLNSQYYFAAEFPADSLQAAQPFTIGDNKTYNG YWNTPLLPYKSYRIYFQAASRANGETKIDCVQVATKGAATPKP VPEPEKQTDHTVKIAGVIAGILLFVIIFLGVVLVMKKRLYKHG ASICSASGEASGSFQSWRKAKHKQACPMARAGARERAGGCLKL
652	1391	30	459	GIRQLLQLSRASMAARKSWTALRLCATVVVLDMVVCKGFVQDL DESFKENRNDDIWLVHFYAPWCGHCKKLEPIWNEAGLEMKSIG SPVKAGKMDATSYSSIASEFGVRGYPTIKLALIRPLPSQQMFE HMHKRHRVFFVYV
653	1392	168	1016	GLVIVISHFSPSPGLLPATQSPAMSDPITLNVGGKLYTTSLAT LTSFPDSMLGAMFSGKMPTKRDSQGNCFIDRDGKVFRYILNFL RTSHLDLPEDFQEMGLLRREADFYQVQPLIEALQEKEVELSKA EKNAMLNITLNQRVQTVHFTVREAPQIYSLSSSSMEVFNANIF STSCLFLKLLGSKLFYCSNGNLSSITSHLQDPNHLTLDWVANV EGLPEEEYTKQNLKRLWVVPANKQINSFQVFVEEVLKIALSDG FCIDSSHPHALDFMNNKIIRLIRY
654	1393	3	927	SCADNLVAASGGCWFVLGERRAGSLLSASYGTFAMPGMVLFGR RWAIASDDLVFPGFFELVVRVLWWIGILTLYLMHRGKLDCAGG ALLSSYLIVLMILLAVVICTVSAIMCVSMRGTICNPGPRKSMS KLLYIRLALFFPEMVWASLGAAWVADGVQCDRTVVNGIIATVV VSWIIIAATVVSIIIVFDPLGGKMAPYSSAGPSHLDSHDSSQL LNGLKTAATSVWETRIKLLCCCIGKDDHTRVAFSSTAELFSTY FSDTDLVPSDIAAGLALLHQQQDNIRNNQ\DLPRWSAMPQGAP RKLIWMQN
655	1394	1	716	FRAATAAAKGNGGGGGRAGAGDASGTRKKKGPGPLATAYLVIY NVVMTAGWLVIAVGLVRAYLAKGSYHSLYYSIEKPLKFFQTGA LLEILHCAIGIVPSSVVLTSFQVMSRVFLIWAVTHSVKEVQSE DSVL\FVIAWTITEIIRYSFYTFSLLNHLPYLIKRARYTLFIV LYPMGVSGELLTIYAALPFVRQAGLYSISLPNSTKKIFLISQV WWHMLAVSADAKAAEMPAVLKPGP

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656	1395	72	766	MLTGVGCLVSSESLSCVQCNSWEKSCVNSIASECPSHANTSCI SSSASSSLETPVRLYQNMFCSAENCSEETHITAFTVHVSAEEH FHFVSQCCEGKECSNTSDALDPPLKNVSSNAECPACYESNGTS CRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATC QFLSGENKTLGGVIFRKFECANVNSLTPTSAPTTSHNVGSKAS LYLLALASLLLRGLLP
657	1396	97	746	VPARRRAMEIGTEISRKIRSAIKGKLQELGAYVDEELPDYIMV MVANKKSQDQMTEDLSLFLGNNTIRFTVWLHGVLDKLRSVTTE PSSLKSSDTNIFDSNVPSNKSNFSRGDERRHEAAVPPL\AIPS ARPEKRDSRVSTSSQESKTTNVRQTYDDGAATRLMSTV/KPLR EPAPSEDVIDIKPEPDDLIDEDLNFVQEKPLSQKKPTVTLTYG SSR
658	1397	155	560	ASRVLAAVMGLPWGQPHLGLQMLLLALNWLRPSLSLELVPYTP QITAWDLEGKVTATTFSLEQPRCVFDGLASASDTVWLVVAFSN ASRGFQNPETLADIPASPQLLTDGHYMTLPLSPDQLPCGDPMA GSGSAP
659	1398	416	539	NSLNNFFFETESCCVAQAGVQWRDLGSLQAPPPGFKRFSCL
660	1399	281	736	KSLPLQKHPKPSCQEDQGLGRGSLSGHSPLTLLTFLTSCALGD QQLLPPRTSGSLCQESMSEQSCQMSELRLLLLGKCRSGKSATG NAILGKHVFKSKFSDQTVIKMCQRESWVLRERKVVVIDTPDLF SSIACAEDKQRNIQHLLELSAP
661	1400	2	974	FVETTVSVQSAESSDALSWSRLPRALASVGPEEARSGAPVGGG RWQLSDRVEGGSPTLGLLGGSPSAQPGTGNVEAGIPSGRMLEP LPCWDAAKDLKEPQCPPGDRVGVQPGNSRVWQGTMEKAGLAWT RGTGVQSEGTWESQRQDSDALPSPELLPQDQDKPFLRKACSPS NIPAVIITDMGTQEDGALEETQGSPRGNLPLRKLSSSSASSTG FSSSYEDSEEDISSDPERTLDPNSAFLHTLDQQKPRVVESRSV TQAGVQWHDIGSLQPLPP/WIQAIL/HASAFRIAGTTGACHHA RIIFGFLVERGFHHVGQDGLYLLIL
662	1401	232	3	KICSSYFLRIICILQKEAQEASNLYTSCDFFSPAFYFVIYRLY NFKIHWPGAVAHTYSPSTLGGRGRWVT*GREFM
663	1402	250	556	LILSLPLLYGHLKSYTFPSEHYLHLLQTFATFNKYLNVCVLIF IHHKPVVPAIQGTNVGGSLEPRRLRLQQAMIVPLHFGLGNRVR PCLKKQQQQQQQQQKK
664	1403	1	373	RMETKPVITCLKTLLIIYSFVFWITGVILLAAGVWGKLTLGSY ISLIAENSTYAPYVLIVTGTTIVAYPLV*FFFSYSSGFSYILA VRLIAGIALVYNYIPRSSSRALVRLVVLLRFLLSRHPS
665	1404	3	413	NAEHPGMDRHDLCQKAKLAEHAERDDDMAACMKTVTDQGAELS NEERNLLSDAHTNAV*ARRSSWMGA*RIEQKTEGADTQQQMAP DCREIFATELRDICDDVLSLLEKLLIPNASHA*SLVYYLHMIG DYYRYWL
666	1405	2	334	GGGPLGKMPRAQLADPWQMMAVESPSDCADNGQQIMDEPMGED EISPQTE*VSIKEVAVTHCVKEGHDKADPSQIELLRVLRQGSL GKVYLGKKVSGSDAKQLYAMKVLT

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667	1406	2	332	DAAGIRHEAHFGKLECLVQLVRAGA\SLFVSTTRYAQTPA\HI AAFGGHPQCLVWLIQAGANINKPDCEGETPIHKAARSGSLECI SALVANGAHVDNPKKGIRVLEWLFE
668	1407	242	1157	LLKLMFIAELGDYDLAEHSPELVSEFRFVPIQTEEMELAIFEK WKEYRGQTPAQAETNYLNKAKWLEMYGVDMHVVKARDGNDYSL GLTPTGVLVFEGDTKIGLFFWPKITRLDFKKNKLTLVVVEDDD QGKEQEHTFVFRLDHPKACKHLWKCAVEHHAFFRLRGPVQKSS HRSGFIRLGSRFRYSGKTEYQTTKTNKARRSTSFERRPSKRYS RRTLQMKACATKPEELSVHNNVSTQSNGSQQAWGMRSALPVSP SISSAPVPVEIENLPQSPGTDQHDRKWLSAASDCCQRGGNQWN TRAL
669	1408	278	1	ATAPGLFNFF*FLFQCREEHKKKNPEVPVNFAEFSKKCSGRWK TMSSKEKFKFGEMAKADEVCYDREMKDYGPAKGGKKKDPNAPK RPPSGF
670	1409	139	646	AEGLGSWAVWAGLGWAGRHMEAGGATGALGVGSKLPSAFCFPG SSVAMDMFQKVEKIGEGTYGVVYKAKNRETGQLVALKKIRLDL *VLGRPLSYPPWAITTWALPDPFPLSWSPRLTPLGAAQQPLPV LSPVHCLLTSLCRGPDCGVWWMTCQGAQVSIAGALVILWG
671	1410	3	442	LCVSVLCSFSYLQNGWTASDPVHGYWFR\AGDHVSRNIPVATN NPVRAVQEETRDRFHLLGDPQNKDCTLSIRDTRESDAGTYVFC VERGNMKWNYKYDQLSVNVTASQDLLSRYRLEVPESVTVQEGL CVSVP/WQCPLPPLQLDCL
672	1411	84	836	QLQLCQNCTKRGECHCVPFDTYIKTKKEKKRLSVLPPTRLMEA RFSPINQILPWCRQDLAISISKAINTQEAPVKEKHARRIILGT HHEKGAFTFWSYAIGLPLPSSSILSWKFCHVLHKVLRDGHPNV LHDCQRYRSNIREIGDLWGHLHDRYGQLVNVYTKLLLTKISFH LKHPQFPAGLEVTDEVLEKAAGTDVNNM*VTLHGYMASSPRLP HSFLPRLTPRRPHGAVGLNESVALLVDAHAPRDRG
673	1412	307	664	AAPHRMPRAPHFMPLLLLLLLLSLPHTQAAFPQDPLPLLISDL QGTSPLSWLPSLEDDAVAA*LGLDFQRFLTLNRTLLVAARDHV FSFDLQAEEEGEGLVPNKYLTWRSQDVENCAVR*KLTLNRTLL VAARDHVFSFDLQAEEEGEGLVPNKYLTWRSQDVENCAVR
674	1413	24	420	HLVPKTRGRGTPSGDQSPVLTLTP*GDPPTILGPQTNQPKEHL TNFKSGKRSFHSLLQPLLLLLHPSISPFLNFGSFPFLVETEET CFIHKLKTPALVTPDSLPLVFNHCGDACLIIHPHFRDVEFHHT GN

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675	1414	1	1101	CCSTKNISGDKACNLMIFDTRKTARQPNCYLFFCPNEEACPLK PAKGLMSYRIITDFPSLTRNLPSQELPQEDSLLHGQFSQAVTP LAHHHTDYSKPTDISWRDTLSQKFGSSDHLEKLFKMDEASAQL LAYKEKGHSQSSQFSSDQEIAHLLPENVSALPATVAVASPHTT SATPKPATLL\PTNASVTPSGTSQPQLA\TTAPPVTTVTSQPP TTLISTVFTRAAATLQAMATTAVLTTTFQAPTDSKGSLETIPF TEISNLTLNTGNVYNPTALSMSNVESSTMNKTASWEGREASPG SSSQGSVPENQYGLPFEKWLLIGSLLFGVLFLVIGLVLLGRIL SESLRRKRYSRLDYLINGIYVDI
676	1415	178	621	IFAGSGVMRLKISLLKEPKHQELVSCVGWTTAEELYSCSDDHH IVKWNLLTSETTQIVKLPDDIYPIDFHWFPKSLGVKKQTHAES FVLTSSDGKFHLISKLGRVEKSVEAHCGAVLAGRWNYEGTALV TVGEDGQI*IWSKTGMLIS
677	1416	1258	944	ARATTKRHFILLFLFFLRRC\LFLSPRMECNGAILAHCNLHLP GSSSSSASAS*VAGITDVRHHAQLILFVFLVETGFHRVGQAGL KLLTSGDLLTSASQSAGIIMGISHCAQPKKAF*TKTF
678	1417	876	1291	EAGSNDDLAT*KTCGRARPSSRSRQFGSRVWNHRQGVRSSPGE GAGSRSPCRRRHRRKHRRNVQSP*RRRSRSCSRRSGRCSVALL GACPVAGHSRGKVVCRRAHAITQRRRCCGFDPMVHPKEHRG*R ERSRKWSRS
679	1418	262	539	ATAPGLFNFF*FLFQCREEHKKKNPEVPVNFAEFSKKCSGRWK TMSSKEKFKFGEMAKADEVCYDREMKDYGPAKGGKKKDPNAPK RPPSGF
680	1419	104	236	LTVNYVLVFSRDSGLRAIENLMQKKGKFDYILLETTGLADPGK K
681	1420	3	277	HEAALCRTRAVAAERHFLRVFLFFRPFRGVGTESGSESGSSKA KEPRTPSSSYGTAQYRRWPIAQEYKHCTAHNDTGTLCSELREP WRRPQ
682	1421	3	576	EGSSQANTLRSRKENRNNLLACLESHVLR*QFTESHLCSLMGD NPFQPKSNSKMAELFMECEEEELEPWQKKVKEVEDDDDDEPIF VGEISSSKPAISNILNRVNPSSYSRGLKNGALSRGITAAFKPT SQHYTNPTSNPVPASPINFHPESRSSDSSVIGQPFSKPVSVSK TIRPAQGSIGCCLSISTV
683	1422	6	627	CFSLEDILNFFLQGFSAGLFAFYHDKDGNPLTSRFADGLPPFN YSLGLYQWSDKVVRKVERLWDVRDNKIVRHTVYLLVTPRVVEE ARKHFDCPVLEGMELENQGGVGTELNHWEKRLLENEAMTGSHT QNRVLSRITLALMEDTGRQMLSPYCDTLRSNPLQLTCRQDQRA VAV\CNLQKFPKPLPQEYQYFDELSGIPAEDLPYYG

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corre-sponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
684	1423	1	1272	AARRRRQLVSRRRTAE\YPRRRRSSPSARPPDVPGQQPKAAKS PSPVQGKKSPRLLCIEKVTTDKDPKEEKEEEDDSALPQEVSIA ASRPSRGWRSSRTSVSRHRDTENTRSSRSKTGSLQLICKSEPN TDQLDYDVGEEHQSPGGISSEEEEEEEEEMLISEEEIPFKDDP RDETYKPHLERETPKPRRKSGKVKEEKEKKEIKVEVEVEVKEE ENEIREDEEPPRKRGRRRKDDKSPRLPKRRKKPPIQYVRCEME GCGTVLAHPRYLQHHIKYQHLLKKKYVCPHPSCGRLFRLQKQL LRHAKHHTDQRDYICEYCARAFKSSHNLAVHRMIHTGEKPLQC EICGFTCRQKASLNWHMKKHDADSFYQFSCNICGKKFEKKDSV VAHKAKSHPEVLIAEALAANAGALITSTDILGTNPES
685	1424	56	526	MTANRLAESLLALSQQEELADLPKDYLLSESEDEGDNDGERKH QKLLEAISSLDGKNRRKLAERSEASLKVSEFNVSSEGSGEKLV LADLLEPVKTSSSLATVKKQLSRVKSKKTVELPLNKEEIERIH REVAFNKTAQVLSKWDPVVLKNRQAEQL*
686	1425	132	344	RIDFMFHSSAMVNSHRKPMFNIHRGFYCLTAILPQICICSQFS VPSSYHFTEDPGAFPVATNGERFPWQELRLPSVVIPLHYDLFV HPNLTSLDFVASEKIEVLVSNATQLIILHSKDLEITNATLQSE EDSRYMKPGKELKVLSYPAHEQIALLVPEKLTPHLKYYVAMDF QAKLGDGFEGFYKSTYRTLGGETRILAVTDFEPTQARMAFPCF DEPLFKANFSIKIRRESRHIALSNMPKVKTIELEGGLLEDHFE TTVKMSTYLVAYI/DL*FPLMGNDFLGRS
687	1426	3	678	RSKIPRSDPRVRTPAPAEAEQGKSQCPSGSTAQSWSAMDILVP LLQLLVLLLTLPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNR KMESKKRELFSQIKGLTGASGKVALLELGCGTGANFQFYPPGC RVTCLDPNPHFEKFLTKSMAENRHLQYERFVVAPGEDMRQLAD GSMDVVVCTLVLCSVQSPRKVLQEVRRVLRPGGVLFFWEHVAE PYGSWAFMW
688	1427	240	641	RLQNSSLMDPKLGRMAASLLAVLLLLLLERGMFSSPSPPPALL EKVFQYIDLHQDEFVQTLKEWVAIESDSVQPVPRFRQELFRMM AVAADTLQRLGARVASVDMGPQQLPDGQSLPIPPVILAELGSD PTKG
689	1428	1	116	FFFFEMESCSVTQAGVPWHDLSSLQPPPPRFKRFSCLS
690	1429	75	511	DPKAQLPEPLRVLWTAHLVAMAPGSRTSLLLAFALLCLPWLQE AGAVQTVPLSRLFDHAMLQAHRAHQLAIDTYQEFEETYIPKDQ KYSFLHDSQTSFCFSDSIPTPSNMEETQQKSNLELLRISLLLI ESWLEPVRILMSIVPN

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691	1430	2	1364	FVKLIKKHQAAMEKEAKVMSNEEKKFQQHIQAQQKKELNSFLE SQKREYKLRKEQLKEELNENQSTPKKEKQEWLSKQKENIQHFQ AEEEANLLRRQRQYLELECRRFKRRMLLGRHNLEQDLVREELN KRQTQKDLEHAMLLRQHESMQELEFRHLNTIQKMRCELIRLQH QTELTNQLEYNKRRERELRRKHVMEVRQQPKSLKSKELQIKKQ FQDTCKIQTRQYKALRNHLLETTPKSEHKAVLKRLKEEQTRKL AILAEQYDHSINEMLSTQALRLDEAQEAECQVLKMQLQQELEL LNAYQSKIKMQAEAQHDRELRELEQRVSLRRALLEQKIEEEML ALQNERTERIRSLLERQAREIEAFDSESMRLGFSNMVLSNLSP EAFSHSYPGASGWSHNPTGGPGPHWGHPMGGPPQAWGHPMQGG PQPWGHPS\GPMQ\GVPR/GSSMGVR
692	1431	50	504	LAHGSFGVSDFPAPAAAPAHTLTSFSGSLSPQFRKPLGRAPAM PLVRYRKVVILGYRCVGKTSLAHQFVEGEFSEGYDPTVENTYS KIVTLGKDEFHLHLVDTAGQDEYSILPYSFIIGVHGYVLVYSV TSLHSFQVIESLYQKLHEGHGK
693	1432	130	1671	SSPSRELCFYGFWIASSWWSRWVGSLGPGILPSPPARGRTFAS VSRLPPPWSAGITLTPFLICQSGSVCPGLGAGFGVRSFHHPVA RSAVLLLPLAPAAAQDSTQASTPGSPLSPTEYERFFALLTPTW KAETTCRLRATHGCRNPTLVQLDQYENHGLVPDGAVCSNLPYA SWFESFCQFTHYRCSNHVYYAKRVLCSQPVSILSPNTLKEIEA SAEVSPTTMTSPISPHFTVTERQTFQPWPERLSNNVEELLQSS LSLGGQEQAPEHKQEQGVEHRQEPTQEHKQEEGQKQEEQEEEQ EEEGKQEEGQGTKEGREAVSQLQTDSEPKFHSESLSSNPSSFA PRVREVESTPMIMENIQELIRSAQEIDEMNEIYDENSYWRNQN PGSLLQLPHTEALLVLCYSIVENTCIITPTAKAWKYMEEEILG FGKSVCDSLGRRHMSTCALCDFCSLKLEQCHSEASLQRQQCDT SHKTPFVSPLLASQSLSIGNQVGSPESGRFYGLDLYGGLHM
694	1433	517	578	VSWVPSKDGDVEGARRPFTRLNTSLGPGLQEGRRRTWLVPIPG AVLPGRTQEQPRASPLY*PGAPPCQPQGLVAGPWAQ*AGLRSD GFGPWPW\RLVGTAGPREKKVQKSKCWHFRCGRHPARRSGWAG RHASLLATGRPCSSAPSQQPLGTAGDSRQELLRPPLV*VNGAQ SSAAGDWGSSPRTAQALARPHRLGHHPAAVAPAARLRTQSGHS PRGPLCRSPGSPRRMGTWRGPAGHSHD
695	1434	249	632	KTVAEEASVGNPEGAFMKMLQARKQHMSTELTIESEAPSDSSG INLSGFGSEQLDTNDESDVSSALSYILPYLSLRNLGAESILLP FTEQLFSNVQDGDRLLSILKNNRKSPSQSSLLGNKFKNKIF
696	1435	333	881	GECFIMAAVVQQNDLVFEFASNVMEDERQLGDPAIFPAVIVEH VPGADILNSYAGLACVEEPNDMITESSLDVAEEEIIDDDDDDI TLTVEASCHDGDETIETIEAAEALLNMDSPGPMLDEKRINNNI FSSPEDDMVVAPVTHVSVTLDGIPEVMETQQVQEKYADSPGAS SPEQPKRKKK

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
697	1436	3	466	HEASGVSRALLQSAPGTPATVGISVGELWPFARCCSHSYVRSL RGLSVSTHLLCFTIYIMNPSMKQKQEEIKENIKTSSVPRRTLK MIQPSASGSLVGRENELSAGLSKRKHRNDHLTSTTSSPGVIVP ESSENKNLGGVTQESFDLMIKGMKK
698	1437	50	241	PLPARGKSTLPATFCSPSAPELASMSVVPPNRSQTGWPRGVTQ FGNKYIQQTKPLTLERTINL
699	1438	1	422	AEGEDVPPLPTSSGDGWEKDLEEALEAGGCDLETLRNIIQGRP LPADLRAKVWKIALNVAGKGDSLASWDGILDLPEQNTIHKDCL QFIDQLSVPEEKAAELLLDIESVITFYCKSRNIKYSTSLSWIH LLKPLVHLQLP
700	1439	161	413	ALPKFLTHGVKSNERVVVWLFPPSFRAATMVHMNVLPDALKSI NNAERRGKPQVLIRLCSKIIIWFLTVMVKYGYIGKFEPTRP
701	1440	211	977	AMAQYGHPSPLGMAAREELYSKVTPRRNRQQRPGTIKHGSALD VLLSMGFPRARAQKALASTGGRSVQAACDWLFSHVGDPFLDDP LPREYVLYLRPTGPLAQKLSDFWQQSKQICGKNKAHNIFPHIT LCQFFMCEDSKVDALGEALQTTVSRWKCKFSAPLPLELYTSSN FIGLFVKEDSAEVLKKFAADFAAEAASKTEVHVEPHKKQLHVT LAYHFQASHLPTLEKLAQNIDVKLGCDWVATIFSRDIRFA
702	1441	3	408	QTRPASPRTARESVLGVSQNMSFNLQSSKKLFIFLGKSLFSLL EAMIFALLPKPRKNVAGEIVLITGAGSGLGRLLALQFARLGSV LVLWDINKEGNEETCKMAREAGATRVHAYTCDCSQKEGVYRVA DQVKK
703	1442	708	244	MVARKGQKSPRFRRVTCFLRLGRSTLLELEPAGRPCSGRTRHR ALHRRLVACVTVSSRRHRKEAGRGRAESFIAVGMAAPSMKERQ VCWGARDEYWKCLDENLEDASQCKKLRSSFESSCPQQWIKYFD KRRDYLKFKEKFEAGQFEPSETTAKS
704	1443	3	475	PAPAARSRELLKELRNGQDMDTVVFEDVVVDFTLEEWALLNPA QRKLYRDVMLETFKHLASVDNEAQLKASGSISQQDTSGEKLSL KQKIEKFTRKNIWASLLGKNWEEHSVKDKHNTKERHLSRNPRV ERPCKSSKGNKRGRTFRKTRNCNRHLRR
705	1444	276	437	CVCGFFVCFETKSCFVAQAGVQWHNLSSLQALPPGFKQFSCLS LLSSWHYRRV
706	1445	2	322	GTRLRRRREAVWFEVVNMDFSRLHMYSPPQCVPENTGYTYALS SSYSSDALDFETEHKLDPVFDSPRMSRRSLRLATTACTLGDGE AVGADSGTSSAVSLKNRAAR
707	1446	123	410	DTMQAVVPLNKMTAISPEPQTLASTEQNEVPRVVTSGEQEAIL RGNAADAESFRQRFRWFCYSEVAGPRKALSQLWELCNQWLRPD IHTKE\QILE
708	1447	2	384	PICLFSRPTLRPSRSKVSLIEGRGANMAARWRFWCVSVTMVVA LLIVCDVPSASAQRKKEMVLSEKVSQLMEWTNKRPVIRMNGDK FRRLVKAPPRNYSVIVMFTALQLHRQCVVCKYELQLRFKIK

SEQ ID NO: of Nucleic Acids	SEQ ID NO: of Amino Acids	Predicted beginning nucleotide location corresponding to first amino acid residue of amino acid sequence	Predicted end nucleotide location corresponding to first amino acid residue of amino acid sequence	Amino acid segment containing signal peptide (A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine, X=Unknown, *=Stop Codon, /=possible nucleotide deletion, \=possible nucleotide insertion)
709	1448	104	535	QMRVKDPTKALPEKAKRSKRPTVPHDEDSSDDIAVGLTCQHVS HAISVNHVKRAIAENLWSVCSECLKERRFYDGQLVLTSDIWLC LKCGFQGCGKNSESQHSLKHFKSSRTEPHCIIINLSTWIIWWY EWDEKIFTPLNKKG
710	1449	116	479	AKERGEERQGEGGGWLSGSRWPLVRSAFVPAPSSLILSMCLSP GIPEAAPDSPLTASAPTP*VMLLGDTGVGKTCFLIQFKDGAFL SGTFIATVGIDFRVRWLQALASSREPGLWLRHGGV
711	1450	2	232	FYPRSSADLPFQTTRCEFQTSVMELAHSLLLNEEALAQITEAK RPVFIFEWLRFLDKVLVAANKVWYCSFFPVALT
712	1451	105	393	MNMKQKSVYQQTKALLCKNFLKKWRMKRESLLEWGLSILLGLC IALFSSSMRNVQFPGMAPQNLGRVDKFNSSSLMVVYTPISNLT QQIMNKTAL
713	1452	2	525	SPQGNGCPDVTGDSVIRVPLTLLVHNLAGLTGLLHHCLSGPLP APSPPPAMSSSRKDHLGASSSEPLPVIIVGNGPSGICLSYLLS GYTPYTKPDAIHPHPLLQRKLTEAPGVSILDQDLDYLSEGLEG RSQSPVALLFDALLRPDTDFGGNMKSVLTWKHRKEHAIPHVVL GR
714	1453	2	1557	NRRTRAQRCQRGRSCGAREEEVEPGTARPPPAASAMDASLEKI ADPTLAEMGKNLKEAVKMLEDSQRRTEEENGKKLISGDIPGPL QGSGQDMVSILQLVQNLMHGDEDEEPQSPRIQNIGEQGHMALL GHSLGAYISTLDKEKLRKLTTRILSDTTLWLCRIFRYENGCAY FHEEEREGLAKICRLAIHSRYEDFVVDGFNVLYNKKPVIYLSA AARPGLGQYLCNQLGLPFPCLCRVPCNTVFGSQHQMDVAFLEK LIKDDIERGRLPLLLVANAGTAAVGHTDKIGRLKELCEQYGIW LHVEGVNLATLALGYVSSSVLAAAKCDSMTMTPGPWLGLPAVP AVTLYKHDDPALTLVAGLTSNKPTDKLRALPLWLSLQYLGLDG FVERIKHACQLSQRLQESLKKVNYIKILVEDELSSPVVVFRFF QELPGSDPVFKAVPVPNMTPSGVGRERHSCDALNRWLGEQLKQ LVPASGLTVMDLEAEGTCLRFSPLMTAAGKPGLVDIPCFCSGA AG
715	1454	319	873	LCIMDTKEEKKERKQSYFARLKKKKQAKQNAETASAVATRTHT GKEDNNTVVLEPDKCNIAVEEEYMTDEKKKRKSNQLKEIRRTE LKRYYSIDDNQNKTHDKKEKKMVVQKPHGTMEYTAGNQDTLNS IALKFNITPNKLVELNKLFTHTIVPGQVLFVPDANSPSSTLRL SSSSPGATVSPSS
716	1455	60	681	SAGGDSCRAVPMLRFPTCFPSFRVVGEKQLPQEIIFLVWSPKR DLIALANTAGEVLLHRLASFHRVWSFPPNENTGKEVTCLAWRP DGKLLAFALADTKKIVLCDVEKPESLHSFSVEAPVSCMHWMEV TVESSVLTSFYNAEDESNLLLPKLPTLPKNYSNTSKIFSEENS DEIIKLLGDVRLNILVLGGSSGFIELYAYGMFKI
717	1456	357	658	PRDPVTDRARAMPRRGLVAGPDLEYFQRHYFTPAEVAQHNRPE DLWVSYLGRVYDLTSLAQEYKGNLLLKPIVEVAGQDISHWFDP KTRDVSYAGTWDCG

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718	1457	2	481	RIPGRRFRAAFVLGSANVASSVRLRCSFPLSLGGPSGPAAASV ALGPAGPGRSLGRTPDTGDWEMDSVSFEDVAVAFTQEEWALLD PSQKNLYRDVMQEIFRNLASVGNKSEDQNIQDDFKNPGRNLSS HVVERLFEIKEGSQYGETFSQDSNLNLNKI
719	1458	6	469	SLSLSVSPFLRLSLGRVGGMAEEMESSLEASFSSSGAVSGASG FLPPARSRIFKIIVIGDSNVGKTCLTYRFCAGRFPDRTEATIG VDFRERAVEIDGERIKIQLWDTAGQERFRKSMVQHYYRNVHAV VFVYDMTNMASFHSLPSWIEECKQH
720	1459	82	490	RRPSPGSIVIMAAESDVLHFQFEQQGDVVLQKMNLLRQQNLFC DVSIYINDTEFQGHKVILAACSTFMRDQFLLTQSKHVRITILQ SAEVGRKLLLSCYTGALEVKRKELLKYLTAASYLQMVHIAEKR TEAFVKF
721	1460	48	708	AEGLQSAAGIRIDTKAGPPEMLKPLWKAAVAPTWPCSMPPRRP WDRQAGTLQVLGALAVLWLGSVALICLLWQVPRPPTWGQVQPK DVPRSWEHGSSPAWEPLEAEARQQRDSCQLVLVESIPQDLPSA AGSPSAQPLGQAWLQLLDTAQESVHVASYYWSLTGPDIGVNDS SSQLGEALLQKLQQLLGRNISLAVATSSPTLARTSTDLQVLAA RGAH
722	1461	436	677	RKKKMPLPFGLKLKRTRRYTVSSKSCLVARIQLLNNEFVEFTL SVESTGQESLEAVAQRLELREVTYFSLWYYNKQNQRR
723	1462	45	569	LQPLSSWESASEVTRSPVSPEDVKQATSNFENLQKQLARKMKL PIFIADAFTARAFRGNPAAVCLLENELDEDMHQKIAREMNLSE TAFIRKLHPTDNFAQSSCFGLRWFTPASEVPLCGHATLASAAV LFHKIKNMNSTLTFVTLSGELRARRAEDGIVLDLPLYPAHPQD FHE*
724	1463	79	530	AADTMQSDDVIWDTLGNKQFCSFKIRTKTQSFCRNEYSLTGLC NRSSCPLANSQYATIKEEKGQCYLYMKVIERAAFPRRLWERVR LSKNYEKALEQIDENLIYWPRFIRHKCKQRFTKITQYLIRIRK LTLKRQRKLVPLSKKVERREK
725	1464	2	261	FVERGLGDPALPTLMFEEPEWAEAAPVAAGLGPVISRPPPAAS SQNKVSDSREQWELFQAAKRTLVDPSAVCIAGRDTCGTVKGES
726	1465	1	860	VVEFLWSRRPSGSSDPRPRRPASKCQMMEERANLMHMMKLSIK VLLQSALSLGRSLDADHAPLQQFFVVMEHCLKHGLKVKKSFIG QNKSFFGPLELVEKLCPEASDIATSVRNLPELKTAVGRGRAWL YLALMQKKLADYLKVLIDNKHLLSEFYEPEALMMEEEGMVIVG LLVGLNVLDANL\CLKGEDLDSQVGVIDFSLYLKDVQDLDGGK EHERITDVLDQKNYVEELNRHLSCTVGDLQTKIDGLEKTNSKL QERVSAATDRICSLQEEQQQLREQNELIR
727	1466	69	452	GCYAPSPHLGGSLTPRFFPNGVFHRRLPRPRPPQPPSVSSAPT LRPLCAHFSLGKLRLRVRKSAEVAPPRTEKGWGSAEPRHSRAP LGLQGLRMAASAQVSVTFEDVAVTFTQEEWGQLDAAQRTLY

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728	1467	1	439	FRGSLSSPSSLRGRRLVTGQTSPRGTWCLYPGFCRSVACAMPC CSHRSCREDPGTSESREMDPVVFEDVAVNFTQEEWTLLDISQK NLFREVMLETFRNLTSIGKKWSDQNIEYEYQNPRRSFRSLIEE KVNEIKEDSHCGETFTQ
729	1468	103	236	LNFANSAAFAVTMPQNEYIELHRKRYGFRLDYHEKKRKKQSRE A
730	1469	213	809	SGDLSPAELMMLTIGDVIKQLIEAHEQGKDIDLNKVKTKTAAK YGLSAQPRLVDIIAAVPPQYRKVLMPKLKAKPIRTASGIAVVA VMCKPHRCPHISFTGNICVYCPGGPDSDFEYSTQSYTGYEPTS MRAIRARYDPFLQTRHRIEQLKQLGHSVDKVEFIEMGGTFMAL PEEYRDYFIRNLHDALSGHTSNNIYE
731	1470	264	799	WESDVGEGLRPPPPPPPPGRRRTQEPRARDAATVIFACPAALL ETLIAYGSSSPSFCKHRAARPLIFLLHRLTAEATARCPICALE ARNPGRWGICASWPGMKTPFGKAAAGQRSRTGAGHGSVSVTMI KRKAAHKKHRSRPTSQPRGNIVGCIIQHGWKDGDEPLTQWKGT VLDQLL
732	1471	2	763	RDLGVALEAFQWARAGDCGSGAGRAGGEGVDAGRRVPERQHRG RGGGGEPGRRQRGGRRQ\RSSSRRSGGDGGDEVEGSGVGAGEG ETVQHFPLARPKSLMQKLQCSFQTSWLKDFPWLRYSKDTGLMS CGWCQKTPADGGSVDLPPVGHDELSRGTRNYKKTLLLRHHVST EHKLHEANAQESEIPSEEGYCDFNSRPNENSYCYQLLRQLNEQ RKKGILCDVSIVVSGKIFKAHKNILVAGSRFFKTLYCFS
733	1472	82	523	SLRAAAAMADVTARSLQYEYKANSNLVLQADRSLIDRTRRDEP TGEVLSLVGKLEGTRMGDKAQRTKPQMQEERRAKRRKRDEDRH DINKMKGYTLLSEGIDEMVGIIYKPKTKETRETYEVLLSFIQA ALGDQPRDILCGAADEVL
734	1473	536	110	CNSAESRMDVLFVAIFAVPLILGQEYEDEERLGEDEYYQVVYY YTVTPSYDDFSADFTIDYSIFESEDRLNRLDKDITEAIETTIS LETARADHPKPVTVKPVTTEPQSP\DL\NDAVSS\LRSPIPL\ LLS\CAFVQVGMYFM
735	1474	2	557	FVRGPGEEQAPAFRKPAPGAMGAQVRLPPGEPCREGYVLSLVC PNSSQAWCEITNVSQLLASPVLYTDLNYSINNLSISANVENKY SLYVGLVLAVSSSIFIGSSFILKKKGLLQLASKGFTRAGQGGH SYLKEWLWWVGLLSILSWNAREKVDL*NITF*PQTSCIFFTIT IEKSTFLSYFPTS
736	1475	127	401	ARGSCPTRPRPANGRMAETKDAAQMLVTFKDVAVTFTREEWRQ LDLAQRTLYREVMLETCGLLVSLGHRVPKPELVHLLKHGQELW IVKRG
737	1476	311	790	YTMLRGTMTAWRGMRPEVTLACLLLATAGCFADLNEVPQVTVQ PASTVQKPGGTVILGCVVEPPRMNVTWRLNGKELNGSDDALGV LITHGTLVITALNNHTVGRYQCVARMPAGAVASVPATVTLASE SAPLPPCHGAVPPHLSHPEAPTIHAASCYS

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738	1477	2	421	WGRRRQLVSEAARAQGDPVCSTMSEEEAAQIPRSSVWEQDQQN VVQRVVALPLVRATCTAVCDVYSAAKDRHPLLGSACRLAENCV CGLTTRALDHAQPLLEHLQPQLATMNSLACRGLDKLEEKLPFL QQPSETVVTS
739	1478	256	1250	AKAFTMAESPGCCSVWARCLHCLYSCHWRKCPRERMQTSKCDC IWFGLLFLTFLLSLSWLYIGLVLLNDLHNFNEFLFRRWGHWMD WSLAFLLVISLLGTYASLLLVLALLLRLCRQPLHLHSLHKVLL LLIMLLVAAGLVGLDIQWQQERHSLRVSL/QDCR*L*TPAVRP *EESGEGHWRRAHLTSSCPQATAPFLHIGAAAGIALLAWPVAD TFYRIHRREPKILLLLLFFGVVLVIYLAPLCISSPCIMEPRDL PPKPGLVGHRGAPMLAPENTLMSLRKTAECGATVFETDVMVSS DGVPFLMHDEHLSRTTNVASVFPTRITAHSS

WHAT IS CLAIMED IS:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1-739, a mature protein coding portion of SEQ ID NO:1-739, an active domain of SEQ ID NO: 1-739, and complementary sequences thereof.

2. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide hybridizes to the polynucleotide of claim 1 under stringent hybridization conditions.

3. An isolated polynucleotide encoding a polypeptide with biological activity, wherein said polynucleotide has greater than about 90% sequence identity with the polynucleotide of claim 1.

4. The polynucleotide of claim 1 wherein said polynucleotide is DNA.

5. An isolated polynucleotide of claim 1 wherein said polynucleotide comprises the complementary sequences.

6. A vector comprising the polynucleotide of claim 1.

7. An expression vector comprising the polynucleotide of claim 1.

8. A host cell genetically engineered to comprise the polynucleotide of claim 1.

9. A host cell genetically engineered to comprise the polynucleotide of claim 1 operatively associated with a regulatory sequence that modulates expression of the polynucleotide in the host cell.

10. An isolated polypeptide, wherein the polypeptide is selected from the group consisting of:

(a) a polypeptide encoded by any one of the polynucleotides of claim 1; and

(b) a polypeptide encoded by a polynucleotide hybridizing under stringent conditions with any one of SEQ ID NO:1-739.

11. A composition comprising the polypeptide of claim 10 and a carrier.

12. An antibody directed against the polypeptide of claim 10.

13. A method for detecting the polynucleotide of claim 1 in a sample, comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide of claim 1 for a period sufficient to form the complex; and

b) detecting the complex, so that if a complex is detected, the polynucleotide of claim 1 is detected.

14. A method for detecting the polynucleotide of claim 1 in a sample, comprising:

a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to the polynucleotide of claim 1 under such conditions;

b) amplifying a product comprising at least a portion of the polynucleotide of claim 1; and

c) detecting said product and thereby the polynucleotide of claim 1 in the sample.

15. The method of claim 14, wherein the polynucleotide is an RNA molecule and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.

16. A method for detecting the polypeptide of claim 10 in a sample, comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex; and

b) detecting formation of the complex, so that if a complex formation is detected, the polypeptide of claim 10 is detected.

17. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:

a) contacting the compound with the polypeptide of claim 10 under conditions sufficient to form a polypeptide/compound complex; and

b) detecting the complex, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.

18. A method for identifying a compound that binds to the polypeptide of claim 10, comprising:

a) contacting the compound with the polypeptide of claim 10, in a cell, under conditions sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and

b) detecting the complex by detecting reporter gene sequence expression, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide of claim 10 is identified.

19. A method of producing the polypeptide of claim 10, comprising,

a) culturing a host cell comprising a polynucleotide sequence selected from the group consisting of a polynucleotide sequence of SEQ ID NO: 1-739, a mature protein coding portion of SEQ ID NO: 1-739, an active domain of SEQ ID NO: 1-739, complementary sequences thereof and a polynucleotide sequence hybridizing under stringent conditions to SEQ ID NO: 1-739, under conditions sufficient to express the polypeptide in said cell; and

b) isolating the polypeptide from the cell culture or cells of step (a).

20. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 740-1478, the mature protein portion thereof, or the active domain thereof.

21. The polypeptide of claim 20 wherein the polypeptide is provided on a polypeptide array.

22. A collection of polynucleotides, wherein the collection comprises the sequence information of at least one of SEQ ID NO: 1-739.

23. The collection of claim 22, wherein the collection is provided on a nucleic acid array.

24. The collection of claim 23, wherein the array detects full-matches to any one of the polynucleotides in the collection.

25. The collection of claim 23, wherein the array detects mismatches to any one of the polynucleotides in the collection.

26. The collection of claim 22, wherein the collection is provided in a computer-readable format.

27. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.

28. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising an antibody that specifically binds to a polypeptide of claim 10 or 20 and a pharmaceutically acceptable carrier.